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RADIOLOGY

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Henry Ford Hospital, Detroit 2, Mich.

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Characteristic Bone Lesions in Post-Irradiated Carcinoma of the Cervix[1]

Metastases versus Osteonecrosis

PHILIP RUBIN, M.D., and DUSDEE PRABHASAWAT, M.D.[2]

ALTHOUGH METASTASES to bone from carcinoma of the cervix are considered unusual, they do occur and present in a characteristic fashion which is worth noting because of the diagnostic appearances on the roentgenogram. Frequently the primary lesion is controlled, although distant bone metastases are present but not appreciated. In a recent review of our cases of carcinoma of the cervix, bone metastases were encountered more frequently than radiation osteosclerosis. Radiographic differential diagnosis is critical to management and can be made with little difficulty once the features are appreciated. These film findings have not been adequately documented in the English literature.

REVIEW OF THE LITERATURE

For an entity which is considered uncommon, it is curious how often bone metastasis in carcinoma of the cervix has been documented in the world literature (Table I). The earliest recorded examples date back to 1893, when Albers-Schönberg (1) reported 5 cases of skeletal involvement encountered among 564 patients with cervical carcinoma.

During the first thirty years of the present century, a number of case reports appeared either in statistical reviews of the problems and causes of death in carcinoma of the cervix or in general descriptive articles of bone metastases by pathologists, listing the various sites of the primary tumor. The first adequate radiographic evidence of bone metastases in carcinoma of the cervix was recorded in 1932 by Philipp (25), demonstrating the various modes of spread and appearance of the bony lesions. The gross pathologic skeletal invasion is well correlated with the x-ray findings in some instances.

In the following decade, sporadic case reports continued to appear, stressing the unusual features of bone metastases in carcinoma of the cervix because of their rarity. In 1940, Norgaard (21) in a very lucid presentation again elaborated upon the problems and unique manner of appearance of some of the bony metastases in cervical cancer. The films of his 3 cases illustrate only some of the points to good advantage.

In more recent years, Drescher (9) has reviewed one of the largest experiences with carcinoma of the cervix (2,132 cases) from the point of view of metastases. The incidence of bone metastases was

[1] From the Division of Radiotherapy and Radioisotopes, Department of Radiology, University of Rochester Medical Center, Rochester, N. Y. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4–9, 1960.

[2] Department of Radiology, Sririraj Hospital, Bangkok, Thailand.

TABLE I: REVIEW OF LITERATURE

Date	Author		Date	Author	
1893	Albers-Schönberg	Skeletal metastases in cervical carcinoma (5/564).	1933	Reich	Blood-borne metastases to vertebra.
1909	MacCormack	Statistical report lists 1/241 cases of cervical carcinoma with spine metastases.	1936	Pearson	In describing cause of death in 57 cases of cervical carcinoma mentioned distant metastases in 25 per cent, of which 7 per cent showed bone involvement.
1909	Clairmont	Lists an unusual case of cervical carcinoma metastasizing to right fibula, with pathological fracture.	1937	Burke	Order of distant metastases to other sites in cervical carcinoma: lung, liver, ovary, bone, and other sites.
1919	Moore	One case of bone metastases from uterus.	1937	Millar	Extensive fibular and patellar destruction in a case of cervical carcinoma.
1921	Wertheimer	Found one instance of bone metastases in a group of irradiated and of nonirradiated cervical carcinoma patients.	1939	Dörr	Reported 8 cases with bone metastases to sacrum, ilium, pubic bone, os calcis, and astragalus, with a 2 per cent incidence in cervical carcinoma.
1930	Ford	Unusually high percentage of pelvic bone metastases: 14/24 cases, a 59 per cent incidence.	1940	Barany and Sala	Reported 2 cases, one with radiograph of humeral metastases.
1931	Faerber	Reports 22 cases of skeletal lesions, mainly in the spine with appearance of nodal extension.	1940	Norgaard	Excellent discussion of method of spread of bone metastases; presentation of 3 cases.
1932	Von Oettingen and Helfferich	Report massive sacral destruction due to direct extension in cervical carcinoma. Autopsies show 5 per cent incidence.	1948	Drescher	Report of 31 cases of bone metastases in 2,132 cases of cervical carcinoma, 1.2 per cent incidence.
1932	Rosh	Distant metastases to fibula after three years in a controlled case of cervical carcinoma.	1950	Cantril	Vertebral and skull metastases occurring three and five years post-irradiation.
1932	Philipp	Good radiographic evidence of bone metastases by direct extension, lymphatic, and blood-borne routes in 5 cases.	1955	Maurer	Unusual case of bone metastases simulating multiple myeloma with lytic skull and skeletal metastases.
1933	Warren	Found 5 instances of bone metastases in 132 autopsied cases of cervical carci oma.	1959	Rubin and Prabhasawat	Discuss characteristic pattern of involvement by metastatic bone carcinoma and osteonecrosis in irradiated patients.
1933	Kelly	Distant metastases in humerus from cervical carcinoma.			

found to be 1.2 per cent and radiographs of some of the 31 reported cases are shown.

In perusing the literature, it is apparent that most of the documented cases are in foreign journals, with few well recorded accounts in American or English publications. The best articles (9, 21) to date are in German journals, in which some of the interesting aspects of these metastases are well demonstrated.

No attempt will be made to review bone necrosis occurring following the treatment of carcinoma of the cervix, since this has been done in a number of comprehensive articles (4, 12, 15).

PRESENTATION OF CASES

In a group of 259 cases of carcinoma of the cervix treated by irradiation at Strong Memorial Hospital (Rochester, N. Y.) from 1940 to 1957, 8 instances of bone metastases and 6 cases of osteosclerosis were found. It has not been the policy to have routine skeletal surveys done in such cases, and one wonders if the incidence is not much higher than is at present thought. A brief tabulation of cases is included so that appreciation of the bone lesions in relation to the stage of the carcinoma, the interval between treatment and discovery, and mode of spread can be commented upon.

A. Bone Metastases: In Table II, 10 cases of metastatic bone carcinoma following irradiation are listed. Two of the patients were originally treated elsewhere

TABLE II: BONE METASTASES FROM CARCINOMA OF CERVIX

Case	Age	Stage	Interval (years)	Type of Bone Lesion†			Status of Primary	Spread	Survival after Metastasis	Path. Proof
				Pelvis	Vertebrae	Other				
I.	39	II	1.8	++	0	0	+	DE	Dc̄ 5 mo.	Yes
II.	43	III	2.5	++	0	0	+	DE	Dc̄ 9 mo.	Yes
III.	68	II	3.5	0	+	0	0	LN	Dc̄ 3.5 yr.	No
IV.	31	I	2.1	0	+	+	0	LN	Dc̄ 1 mo.	Yes
V.	28	III	0.5	0	+	+	+	LN	Dc̄ 1 mo.	Yes
VI.	47	III	1.8	0	+	0	+	LN	Dc̄ 3 yr.	Yes
VII.	44	III	0.1	+	0	0	0	H	Dc̄ 1 mo.	Yes
VIII.	59	II	1.1	+	+	+	0	H	Dc̄ 1 mo.	Yes
IX.*	37	II	0.6	0	0	+	0	H	Dc̄ 1 mo.	No
X.*	68	II	14	0	+	0	0	H	As̄ 2.5 yr	No

*Treated elsewhere.
†Symbols: + Lytic lesions. ++ Lytic and blastic lesions. DE. Direct extension. LN. Lymph node metastases. H. Hematogenous. Dc̄. Dead with carcinoma. Ac̄. Alive with carcinoma. As̄. Alive without carcinoma.

TABLE III: OSTEONECROSIS IN CARCINOMA OF THE CERVIX

Case	Age	Stage	Fields	Interval (years)	Type of Bone Lesion†			Status of Primary	Survival‡	Path. Proof
					Femur	Ilium	Pubis			
XI.	48	I	Lateral	4.5	++	0	+	0	Ds̄ 5 yr.	No
XII.	63	I	Lateral	1.3	++	0	+	0	Ds̄ 9.5 yr.	No
XIII.	60	II	Lateral	5.0	++	0	0	0	Ds̄ 6.0 yr.	No
XIV.	40	I	Lateral	4.0	++	0	0	0	As̄ 7.3 yr.	No
XV.	48	I	Oblique	3.4	0	++	++	0	As̄ 5.3 yr.	No
XVI.	60	II	Oblique	4.5	0	++	++	0	As̄ 4.3 yr.	Yes
XVII.*	55		Lateral	4.0	0	++	++	0	Ds̄ 4.5 yr.	Yes

*Treated elsewhere with biased fields.
†Symbols: + Sclerosis. ++ Fracture. Ds̄. Dead without carcinoma. Otherwise as in Table II.
‡From start of therapy.

and were seen at our hospital for metastatic disease only. The age range was from twenty-eight to sixty-eight years and followed the age distribution for the primary lesion. No correlation with the tumor stage was found. The finding of one early Stage I lesion was surprising. The interval between treatment of the primary cervical cancer and the onset of bone pain was as brief as two months and as long as fourteen years. Most cases seem to present within the first three years after therapy. This is in conflict with Cantril's (6) statement that bone metastases occur three to five years after irradiation. The absence of recurrence of primary disease in 60 per cent of our patients is a most interesting point. This does not refer to radiographic but physical findings on pelvic examination. The commonest sites of involvement were the vertebrae and pelvis. Ribs, scapula, and skull have also been involved in this series.

The finding of bone metastases *per se* is usually a poor prognostic sign and death within one month is common, although one patient survived longer than one year (Case VI). The last patient (Case X) appeared so unusual in respect to onset, response to therapy, and continued survival that the diagnosis of metastases to the dorsal spine must be questioned, as it rests on suggestive film evidence alone.

B. Radionecrosis of Bone: Of the 7 cases of osteonecrosis (Table III) seen in the pelvic region following irradiation for carcinoma of the cervix, 6 were treated in this series, representing an incidence of 2.3 per cent. The age range was forty to sixty years and does not support the theory of predisposition to this development after the age of fifty. The lesions were mostly of Stage I or II, which means that long-term survivors are affected. As reflected in the survival column, most patients had lived five years or more and none had recurrence in the pelvis.

The interval from therapy to onset of radionecrosis was one year and three

months to five years. The average case was seen at four years ± six months. The commonest complication was femoral neck fracture, which in one instance was bilateral. Curiously, all of these cases with fracture of the femoral neck were treated through lateral fields, a technic which was abandoned in 1952. Two of the 3 cases of severe pubic bone fractures and iliac crest breaks were in patients treated through oblique fields. Osteitis pubis, which may or may not be related to irradiation, is a lesion of little clinical significance.

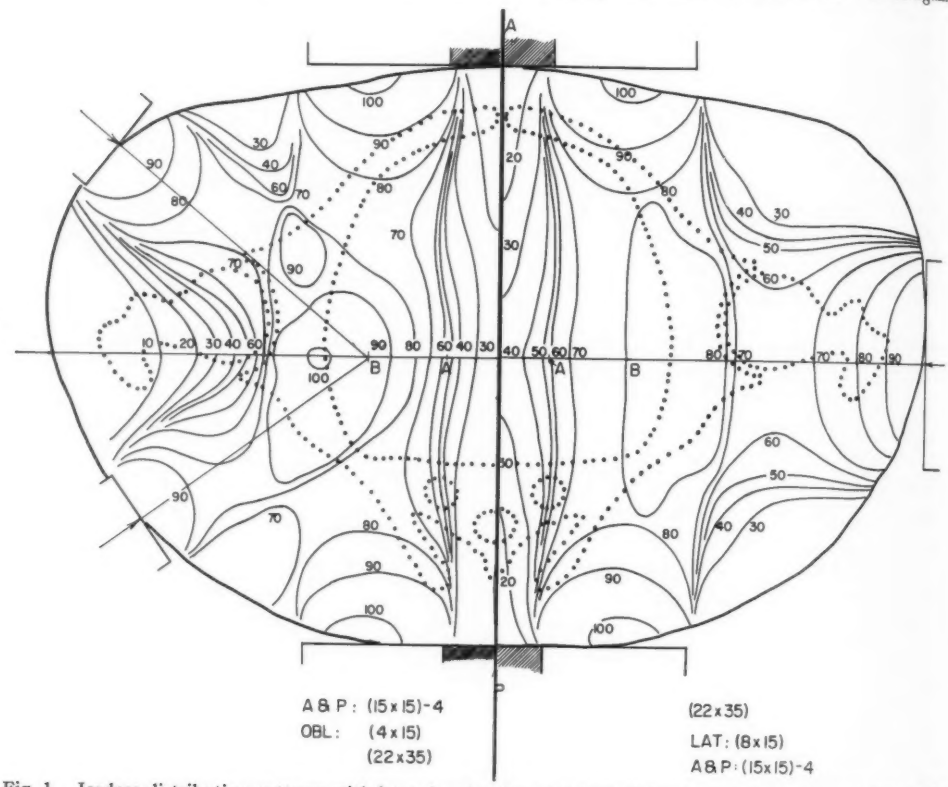

Fig. 1. Isodose distribution patterns with lateral and oblique fields receiving the same skin dose as the anterior and posterior fields, superimposed over the pelvic bones.

Recalculation of isodose curves in these patients suggests some correlation between dose distribution and fracture sites (Fig. 1). In the technic employed from 1940 to 1951 the factors were 280 kv, h.v.l. 1.0 cm. Cu, 6 fields (2 anterior, 2 posterior, and 2 *lateral*) 10 × 15 cm., with a skin dose of 1,600 r each. Each field received the same air dose and the femoral neck was irradiated as uniformly as the rest of the pelvis. From 1952 to 1957, split anterior and posterior fields were used with a 4-cm. midline lead shield, and supplementation was afforded by 2 anterior and posterior *oblique* fields, 15 × 6 cm., to build up the dose to Point B. Once again orthovoltage, 280 kv., h.v.l. 1.1 mm. Cu, was used with a skin dose of 2,400 to 3,000 r depending on patient thickness. Estimated dose in rads with both technics ranged from 7,000 to 12,000 rads. The thinner the patient, the more likely are "hot spots" to occur in the pelvic bones with oblique ports. The one case with iliac crest fracture that was treated with a lateral field had a biased port arrangement. That is, the lateral field received half the dose that the anterior and pos-

terior ports received (1,600 *vs.* 3,200 r, skin). The isodose curves are skewed and simulate our oblique port arrangement. Thus port arrangement is only one of many factors to be considered.

RADIOLOGIC FINDINGS OF BONE METASTASES

As a general rule, the involvement of bone by metastatic carcinoma of the cervix is an osteolytic process. The initial changes are subtle and require careful inspection of roentgenograms, but advancing disease yields a most aggressive and relentless pattern of invasion and bone destruction. Less frequently, there is sclerosis associated with the lytic changes as an expression of reaction to the invading neoplasm. There appear to be three main groups into which the skeletal lesions fall, and one can determine the manner of metastatic spread on the basis of the roentgen appearance and site of the bony lesion.

A. Direct Extension into Pelvic Bones: The earliest changes due to direct invasion of the bony pelvis by parametrial infiltration are along the compact and sharply defined inner cortex which is located between the inferior margin of the sacroiliac joint and the iliac spine near the sacroiliac notch. The initial destruction may be recognized only on comparison with the uninvolved cortex on the opposite side. As the cancer invades more deeply, extensive cortical destruction occurs for several centimeters, the iliopectineal line becomes ragged, and a sharply circumscribed lesion with irregular margins is noted (Figs. 2 and 3). Extension into the sacrum and destruction of the sacroiliac joint have been reported in the literature (25). The acetabular surface of the hip may be destroyed, with intrapelvic protrusion of the femur. The associated sclerosis develops in cases of a more long-standing nature (Fig. 3). The presence of a soft-tissue mass can usually be detected in the area of bone destruction in the pelvis.

CASE I: N. H. W., a 39-year-old woman, entered the hospital with an exophytic mass in the cervix with some invasion of the right parametrial area; classification Stage II.

3-20-57: Treatment was begun with external irradiation, 280 kv, 1 mm. Cu h.v.l., followed by a radium application so that the tumor dose of 7,600 r was delivered to Point A and 5,500 r to Point B in forty-five days.

11-5-57: After a moderate reaction to therapy, which subsided gradually, a tender mass in the rectovaginal septum was felt, which eventually went on to ulceration and formation of a rectovaginal fistula.

5-13-58: Severe pain developed, radiating down the right leg. An extensive recurrence was present in the right adnexal and parametrial areas, reaching the pelvic wall.

12-29-58: Films of the pelvis showed extensive bony destruction near the right sacroiliac joint, associated with a large mass in the pelvis obstructing the right ureter as well (Fig. 2). Treatment for the associated pain was cordotomy rather than radiation therapy.

4-8-59: The patient died with extensive metastases to periaortic nodes, frozen pelvis, hydronephrosis, pyelonephritis, rectovaginal fistula.

Comment: The radiographic findings are compatible with direct extension of the carcinoma into the pelvic bone. The cortical lysis and soft-tissue mass are typical.

B. Retroperitoneal Nodes with Vertebral Destruction: The largest group in the present series consists of those cases with retroperitoneal lymph node metastases along the abdominal aorta, with direct extension into adjacent vertebrae. This starts invariably as a destructive process along the lateral aspects of the bodies of the lumbar vertebrae, usually unilateral in distribution. The incipient changes as recorded by Philipp (26) are of particular interest. Owing to the loss of substance in the vertebral bodies, the articular processes on the affected side are more distinctly seen than those on the uninvolved side (21). Associated with the lytic lesion in bone is a soft-tissue tumescence representing involved retroperitoneal nodes which may be recognized in the loss of definition or bulging of the psoas muscle outline (Fig. 4) and displacement of the kidney and other intra-abdominal organs, as the stomach (Fig. 5).

As the cancer continues to invade, vertebral collapse and rotoscoliosis of the

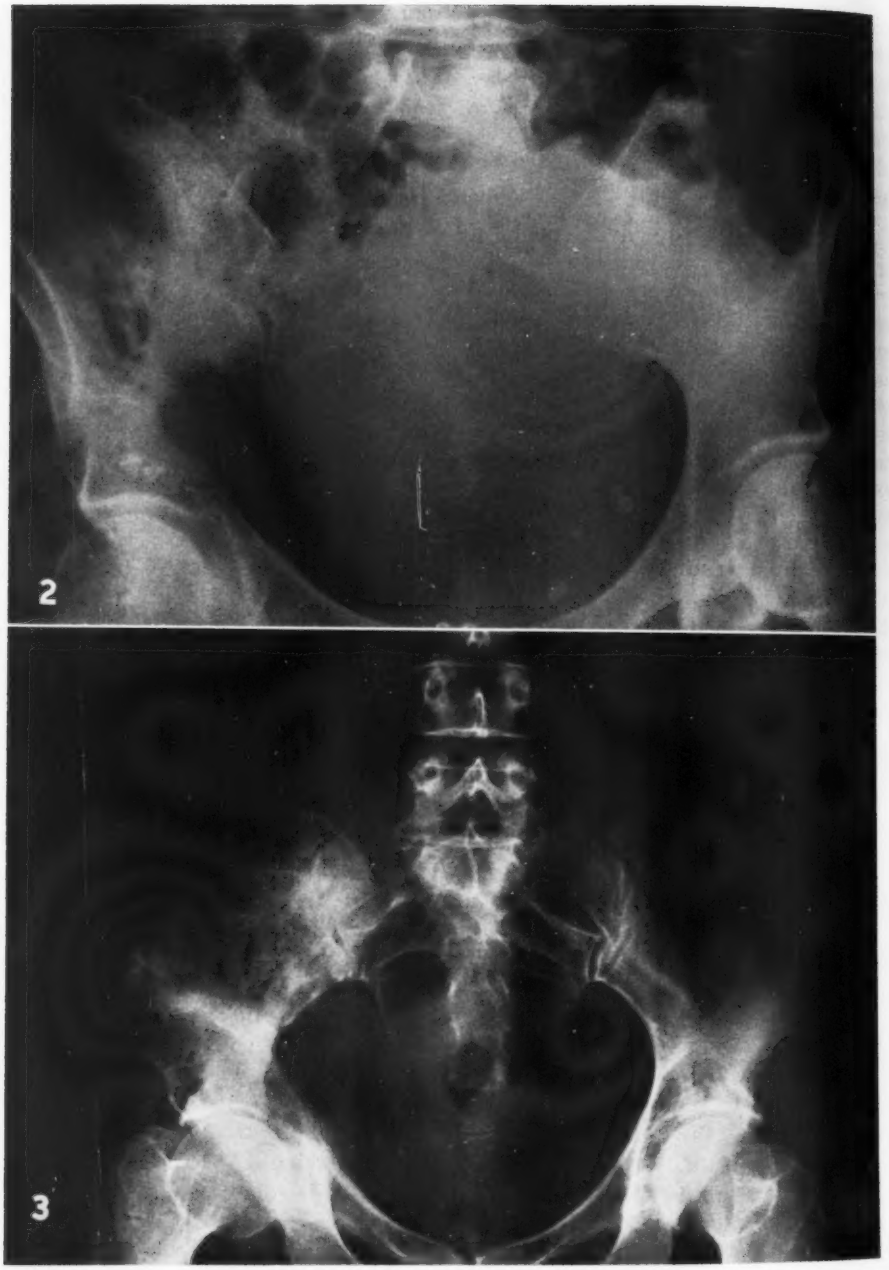

Fig. 2. Case I: Carcinoma of the cervix, Stage II, with direct extension to pelvic wall. Extensive and typical bony destruction of lateral pelvic cortex, iliopectineal line, and sacroiliac joint, with uncontrolled right parametrial disease.

Fig. 3. Case II: Carcinoma of the cervix, Stage III, with direct extension to pelvic wall. Juxtaposed bone shows pattern of lysis of lateral cortex and iliopectineal line, with sclerosis in iliac wing.

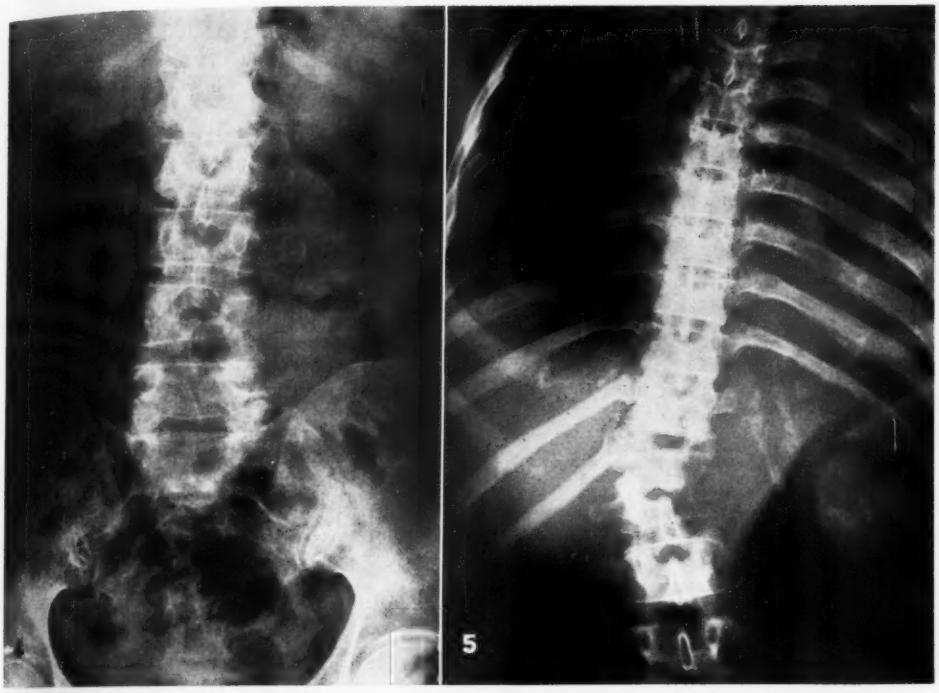

Fig. 4. Case III: Retroperitoneal node metastases from carcinoma of the cervix, Stage II. Note retroperitoneal mass causing bulging of left psoas muscle and destruction of pedicle of L-4. Primary tumor was controlled.
Fig. 5. Case IV: Retroperitoneal node metastases from carcinoma of the cervix, Stage I. Earliest sign of metastases was pleural effusion of unknown etiology. The extensive destruction due to retroperitoneal metastases is seen in adjacent vertebral and rib lysis and displacement of the stomach bubble.

spine occur (Figs. 5 and 6). Adjacent vertebrae become involved and the aggressive nature of the tumor is demonstrated in the extensive and continued destructive pattern of bone invasion on serial films up to the time of death. The loss of intervertebral disk spaces is often mentioned as a differential point against bone metastases but is to be expected in cervical carcinoma. In the thoracolumbar region, the adjacent ribs are grossly eroded by the ingrowth of tumor. The similarity in appearance of bone destruction in Cases IV and V suggests a characteristic picture which has been implied by some authors. This pattern of bone destruction is rarely encountered in other carcinomas with vertebral metastases, since these are not blood-borne.

CASE IV: R. S., a 31-year-old Negress, gave a history of vaginal bleeding due to an early Stage I invasive squamous-cell carcinoma of the cervix.

1-23-51: Treatment was started with an Ernst applicator, followed by external irradiation so that at the end of thirty days the patient received 7,000 r to Point A and 5,000 r to Point B.

4-7-51: Because of a persistent irregularity of the surface of the cervix suggesting residual carcinoma, a hysterectomy was performed, but tissue study showed only radiation effect and no tumor.

8-12-52: Pleural effusion developed, the etiology of which was undetermined.

3-3-53: Because of pain in the back and chest of an unremitting nature, a metastatic survey was done. Evidence of bone destruction was found at the dorsal-lumbar junction with extensive erosion of and collapse of D-12, L-1, and the adjacent ribs on the left side (Fig. 5). In addition, destruction of the 2nd, 3rd, 4th, and 5th ribs was present due to the adjacent pleural disease. No further irradiation was given because of the advanced state of the tumor, and the patient died on 4–17–53.

4-18-53: Autopsy examination revealed generalized metastases with extensive involvement of the lung, left pleura, pericardium and heart, and upper diaphragm, and of the liver, adrenals, and kidneys on the left below the diaphragm. Extensive deposits in the retroperitoneal nodes seemed to

Fig. 6. Case V: Retroperitoneal node metastases from carcinoma of the cervix, Stage III. Similarity to previous case of nodal metastases, with adjacent destruction of vertebrae, disk spaces, and ribs. The calculi-filled gallbladder is displaced by a large retroperitoneal mass.

successfully treated by irradiation followed by hysterectomy, with no sign of disease in the pelvis when the patient was seen with evidence of metastatic disease two years after radiation therapy. The osteolytic destruction was attributed to another primary lesion or to metastasis from some other source rather than arising from the cervical carcinoma.

C. Hematogenous Spread to Other Bones: The roentgen appearance of the hematogenous spread of cervical carcinoma has been well recorded in respect to the lung. The typical lesions in the pulmonary parenchyma are either solitary or multiple nodules, indistinguishable from other metastatic carcinomas to lung. The same holds true of hematogenous metastases to bone except that their rarity makes them of some interest. The simultaneous finding,

Fig. 7. Case VII: Hematogenous spread of carcinoma of the cervix, Stage III. Large lytic lesion in pelvis with preservation of iliopectineal line and lateral cortex suggests hematogenous spread. This is confirmed by negative pelvic examination and simultaneous appearance of nodular pulmonary metastases.

have spread in the vertebrae and up into the chest. Interestingly, no disease was found in the pelvis.

Comment: This is an unusual case of an early Stage I carcinoma of the cervix on a metastatic survey, of an osteolytic lesion in the pelvis (Fig. 7) and metastatic pulmonary nodules suggests blood stream invasion in both cases in our series. It is

of interest to note that this pelvic lesion differs from those due to direct extension in that the lateral cortex and iliopectineal line of the pelvis are intact and the destruction of trabecular pattern is more in keeping with marrow invasion. The ability of these metastases to cross articular cartilage and extend to adjacent bones will be commented on later (Fig. 8).

The number of different skeletal sites reported in the world literature is surprising and indicates that, once vascular spread has occurred, cervical carcinoma can resemble many of the more common carcinomas that metastasize with greater frequency. Most metastases are located in the bones of the lower extremity—the femur, tibia, fibula, patella, os calcis, and astragalus—and pathological fractures are occasionally associated. Of interest once again are the negative pelvic findings and absence of pelvic recurrence in all of our cases in this group.

Fig. 8. Case VIII: Hematogenous spread of carcinoma of the cervix, Stage II. Extensive destruction of pubic bones, with extension into femora across hip joint, peculiar to cervical cancer metastases. Simultaneous appearance of rib, skull, and pulmonary metastases, coupled with a negative pelvic examination, suggests hematogenous spread.

CASE VII. E. S., a 44-year-old woman, was first seen with an extensive carcinoma of the cervix involving the upper vagina, extending bilaterally into the parametrial areas to the pelvic wall; Stage III.

4-23-54: The patient was treated with a combined course of external irradiation and radium, so that a total dose of 7,900 r was delivered to Point A and 4,500 r to Point B in sixty-one days.

6-12-54: Following therapy, the disease in the pelvis was brought under control as evidenced by a negative cervical biopsy in which no tumor cells were found. A metastatic survey, however, revealed an osteolytic lesion in the superior margin of the left acetabulum (Fig. 7). In addition, multiple nodules were found in the pulmonary parenchyma, and the patient died of these distant metastases within the next month.

Comment: This is not the usual picture of pelvic osteolytic bony destruction by direct extension, in that the pelvic cortex was intact. That the metastasis was bloodborne is suggested not only in its presentation but also in the simultaneous appearance of associated metastases in the lungs. There was no evidence of pelvic disease on examination.

RADIOLOGIC FINDINGS IN BONE NECROSIS

With documentation of more than a hundred cases of femoral neck fractures following pelvic irradiation for carcinoma of the cervix, certain facets of this complication are now appreciated. Historically, the patient presents with a spontaneous fracture and no precedent history of trauma can be elicited. As in metastatic bone disease, pain in the groin or knee region may precede the onset of a radiation fracture prior to radiographic detection of change. Roentgen evidence of this lesion in its earliest form is increased bone density and partial cortical fractures (3). In time, the fractures become complete and, if they are unrecognized, displacement of the parts and non-union occur (12) (Fig. 9). True aseptic necrosis of the femoral head is uncommon (15).

Irradiation may lead to sclerosis in other areas of the pelvis. Early changes consist in a fine sclerosis of the trabecular pattern, fanning into the ilium from the sacroiliac joint (Fig. 10). The appearance is not unlike osteitis condensans ilii. Sclerosis may also develop in the pubic bones, simulating osteitis pubis. Fractures of the pubic bones (Figs. 10–12) have occurred less often than in the femoral neck in our series (Table III).

Separation of the pubic synchondrosis was observed in one instance (Fig. 10).

In accordance with the orthopedic axiom that the pelvis always fractures in two places, since it is a "hoop"-like structure, a careful examination of films led to the finding of the other fracture site. In association with pubic-bone fractures and sclerosis, a fracture was identified in the iliac bone. This extended from the iliac crest into the center of the wing in 3 cases (Figs. 10–12). The locations and appearance are so similar as to be virtually pathognomonic. Similarity to a pseudofracture is suggested except for the marked sclerosis of the bone.

Differentiation from metastatic pelvic disease should be no problem. Absence of a pelvic mass has always been noted in this group. The inner cortex and iliopectineal line are preserved. Sclerosis rather than osteolysis is invariably present.

CASE XVI: S. B., a 60-year-old female, entered the hospital with a typical Stage I carcinoma of the cervix.

6-27-55: Treatment consisted of 280-kv irradiation, 1.0 mm. Cu h.v.l., through split anterior and posterior fields and oblique fields so that the estimated dose to Point A was 5,722 r and to Point B 5,576 r. The dose to the pelvic bone was in the order of 12,000 rads.

11-8-58: Onset of pressure pains in the pelvis, with a heavy feeling in the legs; this was worse on sitting, with some relief in lying and standing positions. The symptoms gradually increased in severity until one year later.

9-10-59: Severe dull pain in the pelvic girdle with sharp pain in the medial aspect of both thighs and perineum on certain movements. During the last few months, the patient had been on crutches.

11-27-59: Roentgenogram of the pelvis (Fig. 11) showed an oblique fracture through the left iliac wing; a fracture with callus formation through the left inferior pubic ramus; sclerosis throughout the ilium, and cystic degeneration of the right acetabulum.

12-9-59: Following a bone graft to the pubic area, there was gradual healing. The patient was slowly attempting mobilization and was crutch-walking two months later, quite well and free of pain.

Comment: This example of extensive pelvic bone sclerosis associated with fracture was initially thought to be metastatic in origin. This was the third case in our experience, and the diagnosis was suggested on the basis of films and substantiated on biopsy.

DISCUSSION

The importance of recognizing the true nature of bone lesions in the post-irradiated patient with carcinoma of the cervix is twofold to the radiologist. First, there are the diagnostic problems and therapeutic implications which apply to the patient. Secondly, the frequent absence of recurrent pelvic cancer both in the patients with metastases and with osteonecrosis eliminates clinical findings as a decisive factor in all cases.

From the diagnostic point of view, the question of another primary lesion was raised in Cases III, IV, and VIII, since the pelvic process was controlled. Norgaard has reported a similar clinical experience in which metastatic bone disease proved to be the only sign of cancer on physical examination. As demonstrated, the roentgen appearance is quite typical and the diagnostic features are worthy of emphasis.

The characteristic finding on films of bony destruction in carcinoma of the cervix is a reflection of its mode of spread. It is well appreciated that the commonest route of invasion by this tumor is into the parametrial areas and broad ligaments to the pelvic wall and into lymphatics and lymph nodes along pelvic vessels and the abdominal aorta. It is not surprising, therefore, that most reported cases, as well as those in our series, have involved the pelvis and lumbar vertebrae.

The well defined nature of the cases herein recorded is due to the aggressive penetration of the carcinoma in juxtaposed bone. The earliest changes are a result of direct invasion of vertebrae and may render the articulation processes and pedicles more prominent on the involved side due to loss of substance in the overlying body. This is in contrast to blood-borne vertebral metastases where loss of pedicles may be the first finding of diagnostic im-

Fig. 9. Case XIV: Carcinoma of the cervix, Stage I. Extensive sclerosis of femoral neck associated with fracture on left and early cortical break on right side four years after irradiation.

Fig. 10. Case XV: Carcinoma of the cervix, Stage I. Sclerosis of iliac wings fanning out from sacroiliac joint, associated with fractures of pubis and iliac wing. Separation of pubic synchondrosis and osteitis pubis.

portance. The subtle cortical changes along the sacrosciatic notch in the pelvis or loss of the iliopectineal line are often associated with a soft-tissue mass. Invasion of joints and narrowing of intervertebral spaces are likewise not uncommon

and once again emphasize direct invasion of bone adjacent to cancer-infiltrated tissues rather than blood-borne metastases.

The hematogenous spread should be noted from the diagnostic radiographic point of view apart from its rarity. The ability of metastatic lesions to cross joint spaces and invade articular cartilage is unusual (Case VIII). A curious feature shared by hematogenous metastases with the other two groups (direct extension and lymph-node metastases) is the ability to invade extensively in the new local area. Millar (18) reported a case of massive destruction of tibia, fibula, and patella, and Dörr (8) an instance where adjacent tarsal bones were involved. The most unusual case report of hematogenous spread recorded (17) is one simulating multiple myeloma with multiple punched out skull and skeletal metastases. Perhaps if more skeletal surveys were obtained during the follow-up period of patients with this disease, the incidence would be found to be greater. Some support of this statement may be found in the higher incidence of skeletal metastases in autopsied series—5 to 7 per cent as compared to 1 to 2 per cent in most clinical series.

Accuracy in diagnosis is essential before the proper type of therapy can be instituted. Smithers (29) reports a case of severe acetabular changes and fracture due to repeated courses of irradiation for what was mistakenly thought to be bone metastases. Murphy (20) observed a similar catastrophe in retreatment of lesions thought to be metastases. The radiographic appearance of radiation osteitis is usually that of sclerosis of bone rather than osteolysis. Fractures commonly occur in the femoral neck and pubic rami, points of stress in weight-bearing, and rarely are these to be mistaken for pathologic fracture. In cases of doubt, an attempt at aspiration biopsy is always required to establish a firm diagnosis if a repeat course of radiotherapy is contemplated.

If a lesion proves to be metastatic, a course of radiotherapy is worthwhile and will relieve the pain. The usual course is carried to a tumor dose of 2,000 to 3,500 r, depending upon the response, for vertebral lesions and up to 4,000 r for lesions of the extremities. For therapy to be effective, the entire soft-tissue mass, as in retroperitoneal lymph-node metastases, must be included in the treatment field. These doses are palliative and sufficient to hold the patient until her demise. Treatment for pelvic metastases are more of a problem, since these usually represent recurrence of pelvic tumor with sciatic nerve involvement. For relief of pain a dose in the order of 4,000 to 5,000 r is required, and rarely can this be administered unless a year has elapsed since the original therapy. Many times the clinical course and risk of bowel necrosis warrant cordotomy if the pelvis has been heavily irradiated previously. Supervoltage irradiation may be of some advantage in such circumstances.

Impending radiation fractures can best be treated by rest and restriction of weight-bearing. Occasional examples of spontaneous healing of partial femoral neck breaks have been reported (3). More often the problem is care of a fractured femoral neck. As mentioned, irradiation is disastrous when directed to such cases under a mistaken diagnosis of metastasis. Pinning may be effective but non-union may occur, eventually requiring a vitallium cup arthroplasty (15). Pelvic bone fractures are best treated by bed rest and, if necessary, bone grafting. Healing occurs as with other fractures,[3] but callus formation is reduced and union is slow.

Prevention of radiation bone sclerosis and fracture is more effective than any combination of surgical procedures to care for this complication. The fact that this occurs in Stage I or II lesions pre-

[3] Since this article was submitted for publication, a fine article has appeared on the management and relatively successful outcome by orthopedic maneuver of post-irradiation fractures of the femoral neck (Bickel, W. H., Childs, D. S., and Porretta, C. M.: Post-irradiation Fractures of the Femoral Neck. Emphasis on the Results of Treatment. J.A.M.A. 175: 204–212, Jan. 21, 1961).

Fig. 11. Case XVI: Carcinoma of the cervix, Stage II. Extensive pelvic sclerosis, fracture of pubic rami on right, callus formation, cystic degeneration of right acetabulum, and fracture extending inferiorly and medially from left iliac wing.

Fig. 12. Case XVII: Carcinoma of the cervix, Stage II. Fine fracture of left superior ramus of pubis and sclerosis of left iliac wing, with a fracture in the same location as the other cases.

dominantly and poses a serious handicap to the patient must be considered. It is hoped that, with the advent of supervoltage technics and avoidance of differential bone absorption, this complication will be reduced. For orthovoltage irradiation, lateral rather than oblique fields would seem preferable. The reason offered is that pelvic bone fractures cannot be corrected as readily as femoral neck fractures by orthopedic maneuvers. Sacrosciatic ports to supplement anterior and posterior ports would be worth considering if these fractures occur with sufficient frequency in one's experience. In the final analysis, one must accept a certain minimum complication rate to achieve success in the treatment of this carcinoma.

SUMMARY

1. The characteristic appearance of bone metastases and destruction in cervical carcinoma reflects its mode of spread. Three groups are recognized: direct extension, lymph-node involvement, and hematogenous metastases.

2. The changes are mainly a result of direct invasion of bone from adjacent cancer-infiltrated tissues or lymph nodes.

3. In direct extension, the initial changes in pelvic bones are dissolution of the cortex along the sacrosciatic notch or loss of the iliopectineal line.

4. In lymph-node metastases, the earliest vertebral changes are a loss of body substance, rendering the articular processes on the involved side more apparent. Advanced lesions characteristically show extensive destruction of adjacent bones, joints, and intervertebral spaces, associated with a large soft-tissue mass due to aggressive local invasion and spread.

5. Hematogenous metastases are indistinguishable from those of other neoplasms but are worthy of note because of their rarity and aggressiveness.

6. Radionecrosis of the pelvis is readily distinguishable from metastatic involvement because of the absence of osteolysis and cortical destruction coupled with a predictable pattern of bone sclerosis and fracture in femora, pubis, and ilia, depending on portal arrangements.

7. Therapeutic measures are dependent on proper diagnosis and clinical judgment.

260 Crittenden Blvd.
Rochester 20, N. Y.

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SUMMARIO IN INTERLINGUA

Lesiones de Osso, Characteristic de Carcinoma del Cervice post Irradiation

Le apparentia characteristic de metastases e de destruction ossee in carcinoma cervical reflecte le modo de dissemination del morbo. Tres gruppos de casos es a distinguer: Casos de extension directe, casos de affection de nodos lymphatic, e casos de metastase hematogene.

Le alterationes es principalmente le resultato de un invasion directe del osso ab adjacente tissus o nodos lymphatic con infiltration cancerose.

In casos de extension directe, le alterationes initial de osso pelvic es dissolution del cortice al longo del indentation sacrosciatic o perdita del linea illiopectinal.

In casos de metastase ab nodos lymphatic, le primissime alterationes vertebral es perdita de substantia del corpore, de maniera que le processos articular al latere afficite deveni plus apparente. Lesiones in stato avantiate monstra—characteristicamente—extense destruction del ossos, articulationes, e spatios intervertebral adjacente, in association con le formation de un grande massa de tissu molle como resultato de un aggressive invasion e extension local.

Metastases hematogene es indistinguibile ab illos de altere neoplasmas, sed illos merita nostre attention a causa de lor raritate e aggressivitate.

Radionecrose del pelve es prestemente distinguibile ab affectiones metastatic a causa del absentia de osteolyse e destruction cortical, insimul con le predicibile configuration de sclerose ossee e de fracturas in femore, pube, e ilium (in dependentia ab le arrangiamento de portas).

Le mesuras therpeutic es dictate per le correcte diagnose e le judicamento clinic.

Differential Diagnosis of Intradural (Extramedullary) and Extradural Spinal Canal Tumors[1]

JEROME H. SHAPIRO, M.D., MICHAEL OCH, M.D., and HAROLD G. JACOBSON, M.D.

INTRASPINAL tumors are usually readily detected by myelography. However, although the level of the lesion within the spinal canal is accurately determined by this means, a more precise localization is desirable. In order to accomplish this objective, reliable criteria must be established to permit separation of extradural and intradural lesions. The myelographic findings in combination with the changes seen on the plain spine roentgenograms, together with the clinical observations, might then permit prediction of the histologic diagnosis with reasonable accuracy.

This paper is a review of the intraspinal tumors (exclusive of intramedullary lesions) observed at the Montefiore Hospital (New York) in recent years and confirmed by surgery or postmortem examination. In this analysis special attention will be given to the plain-film and myelographic findings noted in the two groups of spinal canal tumors, and criteria for their diagnosis will be presented.

MYELOGRAPHIC TECHNIC

For precise diagnosis, opaque myelography should be combined with fluoroscopy and fluoroscopic spot-filming. Although the level of a mass may be determined by gas myelography, the findings are less accurate than with an opaque medium, which affords a more precise definition of the abnormality. Epidural introduction of gas or an opaque medium for myelography has not been widely used and is limited to the diagnosis of extradural lesions.

In standard subarachnoid myelography an adequate volume of opaque medium is required. In the lumbar region 9 c.c. are recommended, and 9 to 12 c.c. are generally used in the thoracic and cervical segments. The lumbar route is preferable, but cisternal injections may at times be necessary, alone or in conjunction with lumbar injection. A combined lumbar and cisternal procedure may be done when it is desirable to outline the upper and lower limits of an extensive tumor or in a search for additional abnormalities when there is a complete block with lumbar myelography. Fluoroscopic observations are made following the introduction of the opaque material into the subarachnoid space. With proper injection there will be a free flow of the medium in contrast to what is seen with subdural or extradural injection.

Frontal, oblique, and translateral views are obtained. Frequently, the lateral decubitus position may be useful. Inasmuch as the injecting needle is usually left in place during the examination, most patients are studied in the prone position. An opaque medium heavier than spinal fluid will, however, settle to the ventral aspect of the subarachnoid space, with inadequate opacification of the more dorsal aspect. Thus, in some instances, it is desirable to study the patient in the supine position as well. Roentgenographic exposures should, of course, be of adequate penetration to permit visualization of the cord, nerve roots, and any mass within the subarachnoid fluid.

The use of fluoroscopic image intensification as well as of cineradiography may improve myelography by permitting better visualization and a more complete dynamic recording of the study. Cineradiography may be particularly applicable in the thoracic spine.

MYELOGRAPHIC ANATOMY

The dura mater serves as an outer covering for the contents of the spinal canal and

[1] From the Division of Diagnostic Radiology, Montefiore Hospital, New York, N. Y., and the Department of Radiology, New York University, School of Medicine, New York, N. Y. Presented at the Forty-Sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4–9, 1960.

represents an anatomic landmark separating extradural and intradural tumors. The cervical dura is continuous with the intracranial dura, while the caudal extension forms the caudal sac.

The spinal cord, which terminates at L1-L2 is visualized on frontal and lateral projections as a central tubular defect in the opaque column. The presence of the cord permits intradural masses to be subdivided into intramedullary and extramedullary locations.

The subarachnoid fluid completely surrounds the spinal cord in the cervical, thoracic, and upper lumbar spine, and is traversed by the cauda equina in the rest of the lumbar spine. The lateral limits of the subarachnoid space are well seen in the frontal myelogram, closely approximating the dura mater along the inner aspect of the pedicle on either side. The dorsoventral aspects of the spinal canal, however, are less well outlined with opaque medium. In the conventional prone position, translateral films give a better delineation of the ventral portion of the spinal canal, but, as pointed out above, the dorsal aspect of the canal may be incompletely opacified.

REVIEW OF LITERATURE

The high reliability of precise myelographic localization of intraspinal tumors has been stressed by Camp (4), who concluded that extradural, intradural, and intramedullary lesions should be detected with a minimal degree of error.

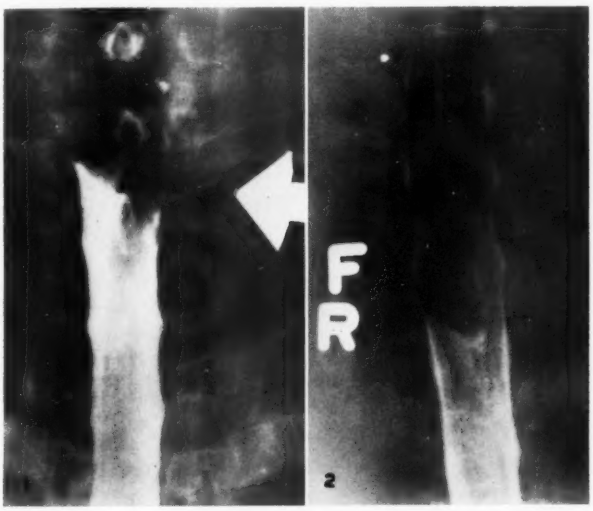

Fig. 1. Intradural neurofibroma, C7-T1, in a 56-year-old man. Marked displacement of spinal cord to the left, with narrowing of left subarachnoid space. Concave defect produced by tumor on right surrounded by a widened subarachnoid space.

Fig. 2. Intradural neurofibroma, T3-T4, in a 37-year-old woman. Spine roentgenograms showed flattening of right pedicles at T3 and T4. Spinal cord widening at level of incomplete block. Central lunate-shaped accumulation of opaque medium representing "capping" of tumor. Otherwise, myelogram has appearance of an intramedullary lesion.

Several large series of intraspinal tumors show surprisingly little variation in the incidence of the different localizations of the neoplasms within the spinal canal. For extradural tumors the incidence is from 20 to 28 per cent; for intradural extramedullary neoplasms the figure is 50 to 60 per cent (12, 14, 17). The proportion of intradural extramedullary to extradural lesions is therefore from 2:1 to 3:1.

According to Schinz (13), intraspinal

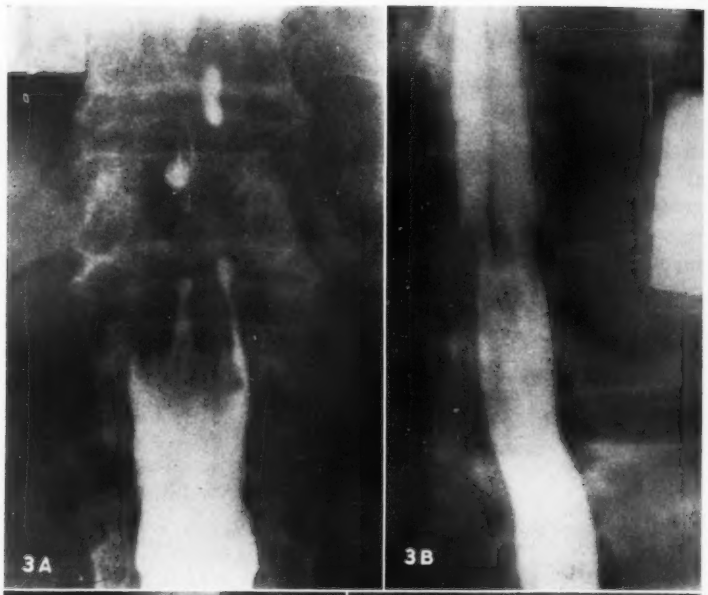

Fig. 3. Intradural neurofibroma, T12-L1 in a 72-year-old man. Spine roentgenograms showed flattening of right pedicle at L1, with an increased interpedicle measurement. A. Incomplete block on frontal myelogram with spinal cord in central position. Small and shallow concave defect on right. B. Lateral myelogram showing no block. Thinning of opaque column at T12-L1, with small defect posteriorly.

Fig. 4. Intradural neurofibromas, T12-L1 and L2, in a 57-year-old woman. A. Roentgenogram of spine showing spreading apart and flattening of pedicles at T12 and L1. B. Marked spinal cord displacement to right. Concave defect on left. Spreading apart of subarachnoid fluid against each pedicle at L1. Additional large central defect below level of block indicates second neurofibroma.

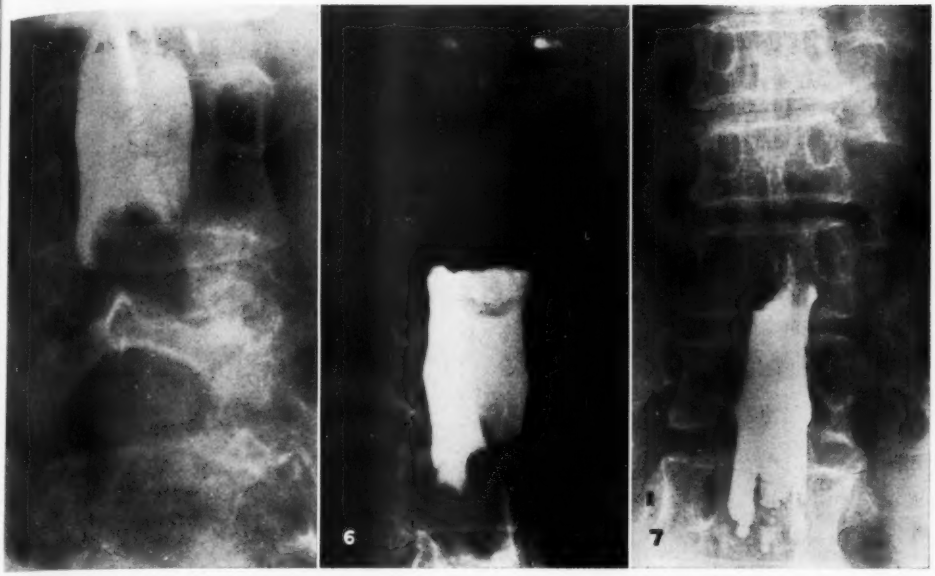

Fig. 5. Intradural neurofibroma, L4-L5, in a 48-year-old woman. Caudal end of the opaque column shows a large central lobulated defect.

Fig. 6. Intradural meningioma, T5, in a woman aged 51. Cisternal myelogram showing compression of spinal cord with marked displacement to left. Concave defect of tumor on right side of cord. The subarachnoid space is considerably increased on the right and almost obliterated on the left.

Fig. 7. Intradural meningioma, T10, in a 62-year-old woman. Marked shift of spinal cord to left. Oblique concave defect of tumor seen on right. Subarachnoid space widened on right and narrowed on left.

tumors display the following findings on the plain films: (*a*) widening of the spinal canal and of the interpediculate distance; (*b*) increased depth of the concave posterior surface of the vertebral body; (*c*) erosion of the neural arches; (*d*) enlargement of the intervertebral foramen; (*e*) paravertebral soft-tissue masses; (*f*) calcification of the tumor; (*g*) abnormal spinal curvature; (*h*) bone destruction or production.

About one-third of all intraspinal neoplasms will show bone changes on preliminary roentgenograms of the spine (4, 12, 14). Bone abnormality occurs in about one-half of the extradural tumors but in only one-fifth of the extramedu lary intradural group (5). In comparing the meningiomas and neurofibromas, there is evidence of the abnormality in 10 per cent of the meningiomas and in almost 50 per cent of the neurofibromas (3). Not only are these changes more frequent in the neurofibromas, but they are also more pronounced than in meningiomas.

Almost all of the meningiomas and neurofibromas are intradural and extramedullary in location, with very few in an extradural position. Sixty to 85 per cent of the meningiomas occur in females (2, 15, 16). The age incidence of the two tumors shows some variation. The average age for meningiomas would appear to be 46.5 years (15). However, in Wood's series (16), all but 2 of the meningiomas were in patients over the age of forty, whereas one-half of the neurofibromas were found below that age. Neurofibromas and meningiomas are most frequently encountered in the thoracic spine, this segment possibly accounting for 60 to 80 per cent of the meningiomas. Of the remainder of this group almost 20 per cent occur in the cervical and 4 per cent in the lumbar spine (2). In the series reported by Rasmussen (12) the distribution of neurofibromas was 18 per cent cervical, 54 per cent thoracic, 21 per cent lumbar, and 7 per cent sacral.

One distinguishing feature of meningiomas is their tendency to calcification,

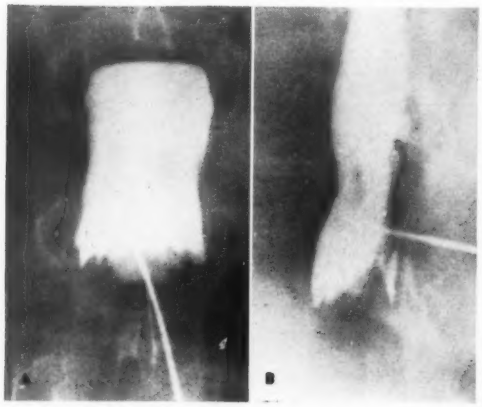

Fig. 8. Intradural meningioma, L2, in a 52-year-old woman. A. Transverse serrated block on frontal myelogram. B. Atypical myelographic deformity similar to that seen with extradural lesions except for dorsal defect on lateral projection.

although Lombardi (10) states that the calcium is rarely sufficient to be demonstrable on roentgenograms of the spine. In one series (2) 15 per cent of the meningiomas were calcified but only 4 per cent could be identified on plain films. Laminagraphy may be useful in such cases. Calcification may be seen also in other tumors, as oligodendroglioma, hemangioblastoma, and teratoma, and with disk herniation (10).

Wood (16) and Tönnis *et al.* (14) found meningiomas and neurofibromas to occur with almost equal frequency.

The myelographic characteristics of the various localizations of intraspinal neoplasms have been well described by several authors (1, 5, 10, 13). In respect to the two localizations discussed in this paper, Begley (1) indicates that extradural tumors usually displace the spinal cord but that displacement is frequently greater with extramedullary intradural lesions. Of all the intradural extramedullary tumors, Lombardi indicates that one-tenth are ventral to the cord, whereas nine-tenths are dorsal and lateral to it.

Wood (17) and Lombardi indicate that extradural tumors are most commonly metastatic, more frequently carcinomas than sarcomas.

The myelographic deformities produced

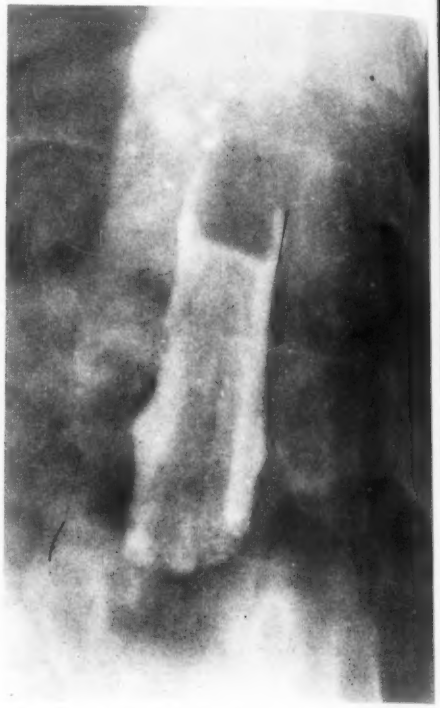

Fig. 9. Intradural sarcoma (seeding from primary neoplasm of cerebellum), T10, in a woman aged 49. The spinal cord is deviated slightly to the right. U-shaped contour of block. Right subarachnoid space closer to right pedicle. Myelographic deformity simulates intramedullary abnormality.

by epidural spinal metastases have been described by Heiser and Swyer (9) and Epstein (6). The former writers emphasized the variation of the extent of the extradural tumor—from an eccentric lesion, lying laterally, dorsally, or ventrally, to annular epidural infiltration. The localization and extent of the extradural process determine the position and degree of compression and displacement of the spinal cord. It will be fixed by concentric lesions, whereas eccentric tumors will displace it away from the mass. Both papers indicate that in the lumbosacral region a large herniated intervertebral disk may offer a serious problem in differential diagnosis.

Törmä (15) and Schinz, in describing myelographic deformities of intraspinal tumors, state that extradural lesions cause the dura to be pressed against the spinal

cord, thus narrowing the subarachnoid space on the side of the tumor. Large tumors may also compress the subarachnoid space on the opposite side. On the other hand, intradural extramedullary tumors cause the dura to be gradually displaced toward the bony margin of the spinal canal. There is dilatation of the subarachnoid space surrounding the mass and outlining it, as well as displacement of the spinal cord away from it. This displacement of the cord results in compression of the contralateral subarachnoid space which, however, may not be narrowed if the tumor is small. With extradural masses the nerve root recesses may not be filled out as often or completely. If the cord is compressed by a tumor located dorsally, the width is increased so that the frontal view may suggest an intramedullary mass.

Orley (11) also has an excellent description of the myelographic deformities in intraspinal tumors. He states that the margin of the opaque material in contact with an extradural tumor is smooth because of the interposition of the dura between the tumor and the medium.

There have been some attempts to distinguish the myelographic deformity in meningiomas and neurofibromas. It is the opinion of Epstein (7) that the deformity is not sufficiently characteristic to permit a differential diagnosis. Wood (16) felt, however, that meningioma and fibroblastoma may be distinguished, inasmuch as the meningioma has a broad attachment with a slightly irregular surface, whereas neurofibromas are more completely surrounded by contrast medium. Neurofibromas, however, may be small, nodular, or lobulated, simulating the irregularity observed with meningioma.

Some specific features of meningiomas are recorded by Lombardi. Myelographically he found them to be well circumscribed but usually not very large. They may displace the spinal cord, sometimes even showing an impression upon it. The tumor is adherent to the dura, with a large broad base, in contrast to the

Fig. 10. Intradural lymphoma, L4-L5, in a man aged 55. Transverse serrated block. Longitudinal defects in opaque column represent cauda equina. Myelographic deformity similar to an extradural lesion, such as a herniated intervertebral disk.

neurofibromas, which are soft masses, although encapsulated. Neurofibromas may depress the cord but not significantly. They are larger than meningiomas and are adherent to one or more of the posterior nerve roots. They may traverse the intervertebral foramina and thus extend into the extradural space. Both meningiomas and neurofibromas may occur as multiple intradural extramedullary tumors.

In the differential diagnosis such entities must be taken into consideration as dilated spinal vessels appearing as defects in the opaque column, arachnoiditis, herniated intervertebral disk, and intramedullary lesions.

PRESENTATION OF MATERIAL

The present series includes 87 intraspinal tumors studied myelographically and confirmed histologically. Surgery or post-

TABLE I: FREQUENCY AND LOCALIZATION OF INTRASPINAL TUMORS

	Cervical	Thoracic	Lumbar	Total
Intraspinal tumors (87 cases)				
Extradural	0	36	15	51 (59%)
Intradural extramedullary	5	23	8	36 (41%)
Meningiomas and neurofibromas (32 cases)				
Meningiomas	4	16	1	21
Neurofibromas	1	6	4	11

mortem examination was performed in all instances. The frequency and localization of the tumors are shown in Table I; 51 of the 87 were extradural. It must be appreciated that Montefiore Hospital has in the past been a large center for neoplastic disease. This fact helps to explain the predominance of the extradural tumors. The incidence of meningioma was double that of neurofibroma.

TABLE II: AGE INCIDENCE OF INTRASPINAL TUMORS

	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90
Extradural	1	1	2	2	6	19	17	1	2
Intradural			1	6*	4	13	7	5	
Meningioma				1	4	7	7	2	
Neurofibroma					3	2	4	2	

* One patient had both a meningioma and a neurofibroma.

The thoracic spine was most frequently involved in both the intradural and extradural group, and by both meningiomas and neurofibromas. The absence of extradural lesions in the cervical portion of the spine is not surprising when one recalls the infrequency of radiographically demonstrable osseous cancer metastases in this area as compared with the thoracic and lumbar segments.

The age incidence of the intraspinal tumors in this series is shown in Table II. The frequency of extradural lesions in the sixth and seventh decades coincides with the incidence of metastatic cancer in this group of patients. Of the intradural lesions, about two-thirds were encountered in the fourth through the sixth decade, with the largest group occurring between the ages of fifty-one and sixty. The meningioma patients tended to be slightly older than those with neurofibroma, the predominant age incidence for meningioma falling between the sixth and eighth decades.

Analysis as to sex incidence (Table III) shows more males than females in the extradural group. By contrast, there were almost two and one-half times as many females as males with intradural tumors. The number of neurofibromas was small, with no significant sex predilection. The meningiomas, however, showed a striking female preponderance, 6 to 1.

TABLE III: SEX INCIDENCE OF INTRASPINAL TUMORS

	Male	Female
Extradural	31	20
Intradural	11	25
Meningioma	3	18
Neurofibroma	6	5
TOTAL	42	45

Table IV lists the histologic types of intraspinal tumors in this series. The most frequent tumor was metastatic carcinoma, followed by meningioma. Lymphoma and neurofibroma occurred with almost equal frequency, with a scattering of the more unusual lesions.

The plain roentgenograms of the spine were studied and the findings are shown in Table V. Abnormalities were considered in two categories: (*a*) paravertebral soft-tissue masses and (*b*) bone involvement (including bone destruction and production). Soft-tissue masses were encountered in 6 of the extradural groups but in none of the intradural series. There was also more frequent involvement of bone by the extradural lesions. This again is readily explained by the fact that the large majority of extradural tumors are extensions to the spinal canal from vertebral involvement by metastatic carcinoma. This type of cancer is particularly prone to involve the body and pedicles of the vertebra. The relative infrequency of

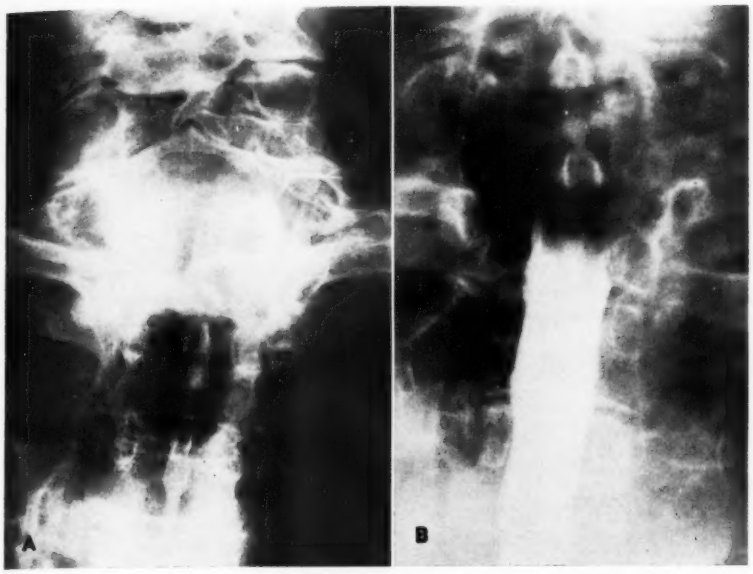

Fig. 11. Extradural myeloma, T1-T2, in a man aged 63. A. Osteolysis and expansion of the neural arches of D1 and D2 seen on frontal roentgenogram of the cervical spine. B. Transverse slightly serrated block with slight displacement of the spinal cord to the left. Displacement of the opaque column away from the right pedicle at the level of the block.

TABLE IV: MICROSCOPIC DIAGNOSIS OF INTRASPINAL TUMORS

Type of Tumor	No. of Cases
Metastatic carcinoma	29
Meningioma	21
Neurofibroma	13
Lymphoma	11
Sarcoma	5
Myeloma	4
Lipoma	1
Ganglioneuroma	1
Hemangioblastoma	1
Malignant melanoma	1
TOTAL	87

TABLE V: INTRASPINAL TUMORS: ABNORMALITIES OBSERVED ON PLAIN ROENTGENOGRAMS OF THE SPINE

Location	Sites of Abnormalities		Vertebral Localization		
	Soft Tissue	Bone	Body	Pedicle	Lamina
Extradural	6	37	31	20	2
Intradural		6		4	2
Meningioma		1		1	
Neurofibroma		4		3	1

bone abnormality in meningioma (1 case) is contrasted with bone involvement in neurofibroma (4 cases).

Our myelographic observations are divided into two categories: the position of the spinal cord and the appearance of the subarachnoid space as outlined by the opaque medium. The myelographic findings in the intradural tumors are shown in Table VI.

TABLE VI: MYELOGRAPHIC FINDINGS IN 36 INTRADURAL EXTRAMEDULLARY TUMORS

	No. of Cases
Position of spinal cord*	
Normal position	6
Displacement	23
Slight	12
Moderate to marked	11
Cup defect	24
Arachnoid closer to pedicles	8
Atypical findings	12
Coarse serrated transverse block	7
Central concave defect	3
"U"-shaped defect	1
Transverse smooth block	1

* Does not include 7 cases with tumor localized below L-1.

The majority of the intradural tumors (80 per cent) caused a displacement of the spinal cord of slight to marked degree. The "cup" or "capping" defect, representing opaque medium surrounding a polypoid mass in the subarachnoid fluid.

TABLE VII: MYELOGRAPHIC FINDINGS IN INTRADURAL EXTRAMEDULLARY TUMORS
(21 Meningiomas; 11 Neurofibromas)

	Meningioma	Neurofibroma
Position of spinal cord		
Normal position	3*	2†
Displacement	17	6
Slight	9	1
Moderate to marked	8	5
Cup defect	17	9
Arachnoid closer to pedicle	5	3
Atypical findings		
Coarse serrated block	4	
Transverse smooth block	1	
No "cup" defect		1

* With exclusion of 1 tumor located below L-1.
† With exclusion of 3 tumors located below L-1.

occurred in 66 per cent of the cases. In 7 cases a coarse serrated transverse block was shown, which did not permit the demonstration of a polypoid mass in the subarachnoid space. In the one instance in which there was a "U"-shaped or central concave defect, the differentiation from an intramedullary mass was difficult, with the tumor in the subarachnoid space fusing with the defect caused by the spinal cord.

In an attempt further to refine the differential diagnosis of intradural extramedullary lesions, comparisons were made between the myelographic findings in patients with meningioma and those with neurofibroma. The results are shown in Table VII. Displacement of the spinal cord was observed with both types of tumor. Although occurring somewhat more frequently with the meningiomas, it was greater with the neurofibromas. The "cup" defect appeared the same in the two lesions. Neither tumor had a distinguishing size or contour. Atypical myelographic findings were encountered in both groups. We feel that there is no distinctive myelographic deformity which would permit a differentiation between meningioma and neurofibroma. Figures 1 to 10 represent the intradural extramedullary tumors.

The myelographic observations in the extradural tumors (Figs. 11–18) were considered as a group and similarly evaluated as to the position of the spinal cord and the appearance of the subarachnoid space. The types of deformity observed are listed in Table VIII. There was a greater tendency in this group of tumors for the spinal cord to remain in normal position and displacement, when present, was

TABLE VIII: MYELOGRAPHIC FINDINGS IN 51 EXTRADURAL TUMORS

	No. of Cases
Typical findings	
Position of spinal cord*	
Normal position	27
Displacement	12
Slight	10
Moderate to marked	2
Transverse serrated block	36
Arachnoid displaced away from pedicle (or bony spinal canal)	44
Atypical findings	9
Smooth transverse block	4
Large central cup defect	2
Smooth convex block	1
Smooth concave block	1
Cup defect	1

* With exclusion of 12 cases in which the tumor was situated below L-1.

generally slight. The most useful sign of an extradural tumor was the displacement of the opaque column from the inner aspect of the bony spinal canal. This was best reflected as a displacement of the subarachnoid fluid from the medial aspect of the pedicle on one or both sides and was seen in about 85 per cent of the cases in this group. The length of the displacement of the subarachnoid fluid varied. A bilateral displacement resulting in a tapering of the opaque column indicates a concentric type of tumor surrounding the dura.

The second most frequent and equally useful sign of extradural tumor was the appearance of a transverse serrated block. This deformity is probably explained by the extrinsic pressure exerted by the extradural mass upon the intraspinal fluid and soft-tissue contents. The compressibility of the subarachnoid fluid and the spinal cord are considered to be factors determining the type of block seen in extradural lesions.

MYELOGRAPHIC PATTERNS IN INTRASPINAL MASS LESIONS

At the conclusion of our myelographic analysis certain patterns emerged which can be used in the differential diagnosis of two anatomic localizations of intraspinal masses.

1. Intradural Masses

A. Position of the Spinal Cord: In that portion of the spinal canal where the cord is present, it may be deviated by an intradural mass toward the contralateral side, away from the tumor. Depending on the size and location of the mass, the deviation may be in a lateral, dorsal, or ventral direction. For that reason, both frontal and lateral roentgenograms are required.

B. Width of the Subarachnoid Space: In contrast to extradural lesions, intradural extramedullary masses cause no separation of the opaque column from the spinal canal. Instead, the column may be displaced toward the bony spinal canal, particularly toward the inner aspect of the pedicles. An intradural extramedullary lesion will widen the opacified subarachnoid space around the mass and there may be compression of the contralateral subarachnoid space.

C. Defects Within the Subarachnoid Fluid: An intradural mass is seen as a defect in the opacified subarachnoid fluid; below the level of the cord, the defect is observed as a radiolucent area in the opaque column. Where the cord is present, the defect is eccentric in position and is attached to the circumferential portion of the opaque column. In contrast to an extradural mass, intradural extramedullary tumors produce sharply outlined filling defects since the opaque material surrounds the mass except for its point of attachment. A sessile or pedunculated lesion can be identified.

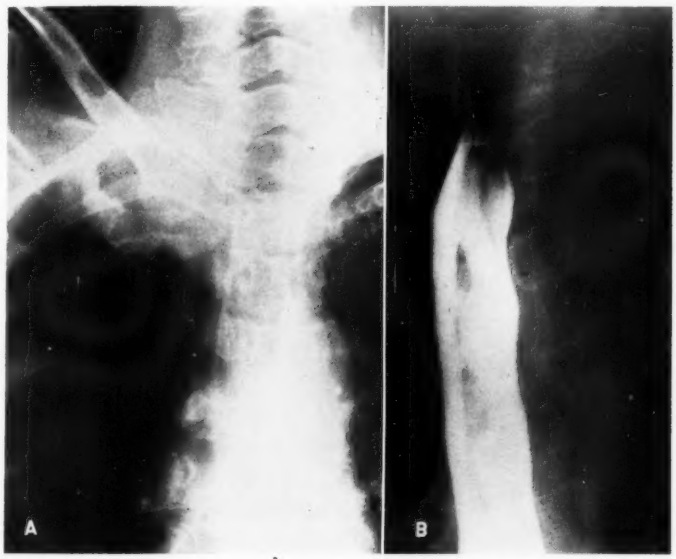

Fig. 12. Extradural neurofibrosarcoma, T2-T3, in a 56-year-old woman. A. Soft-tissue mass in apex of right hemithorax with destruction of right half of vertebral body and pedicle of T2. B. Tapering serrated block with spinal cord slightly shifted to left. Marked separation of opaque column from right pedicle of T3.

D. Contour of the Opaque Column with Complete Block: In contrast to the serrated margin of the opaque column in the presence of an extradural lesion, intradural

extramedullary masses present a diagnostic deformity in those portions of the canal where the cord is present. With complete or almost complete block, in addition to the defect of the spinal cord, an eccentric sharply circumscribed defect seen as a so-called "cupping" or "capping" deformity indicates the precise localization of the abnormality. The cup is formed by the opaque medium outlining the caudal aspect of the polypoid mass (lumbar route myelography). The outer extent of the medium must be carefully determined to make certain that it is not displaced from the bony canal, as with extradural lesions.

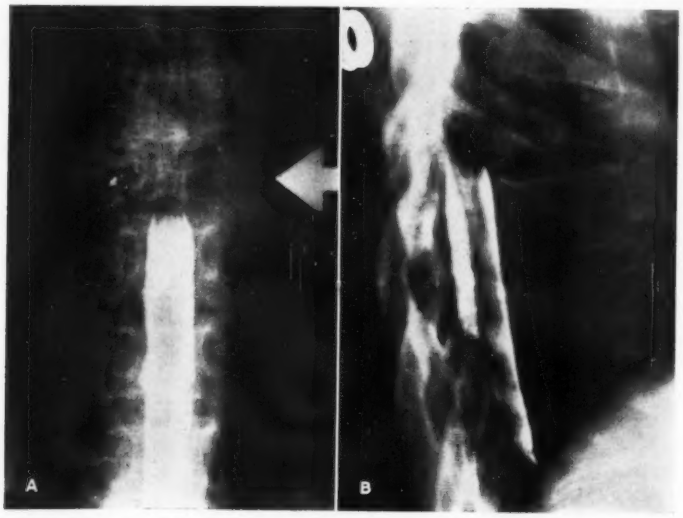

Fig. 13. Extradural myeloma, T7, in a 50-year-old man. A. Collapse of T7 with bilateral paraspinal soft-tissue masses. B. Dorsal displacement of spinal cord on lateral myelogram. Serrated slightly tapering block.

2. *Extradural Masses*

A. Displacement of the Opaque Column from the Inner Aspect of the Spinal Canal and in Particular from the Inner Aspect of the Pedicle: Displacement of the opaque column indicates an extra-arachnoid mass, which is almost always extradural in position. This is best seen in the frontal projection but may also be demonstrated in oblique and lateral views. In the lateral projections, the displacement may be away from the vertebral body or the neural arch. A narrowing of the opaque column results. If the lesion surrounds the spinal canal this narrowing or tapering is more pronounced. The deformity is eccentric if the mass is unilateral.

A special situation is encountered in the caudal sac, which normally shows considerable variation in length. If the sac terminates at a level above the lumbosacral junction, the possibility of an extradural abnormality may be suspected. An extradural mass which results in a shortening of the sac may be confirmed by its irregularity in contour or asymmetry on opacification. A search should be made for any contiguous bone abnormality, which is frequently seen with an extradural tumor.

B. Position of the Spinal Cord: An eccentric extradural mass of sufficient size will displace the spinal cord in the opposite direction. Concentric lesions will tend to fix the cord in its central position. When

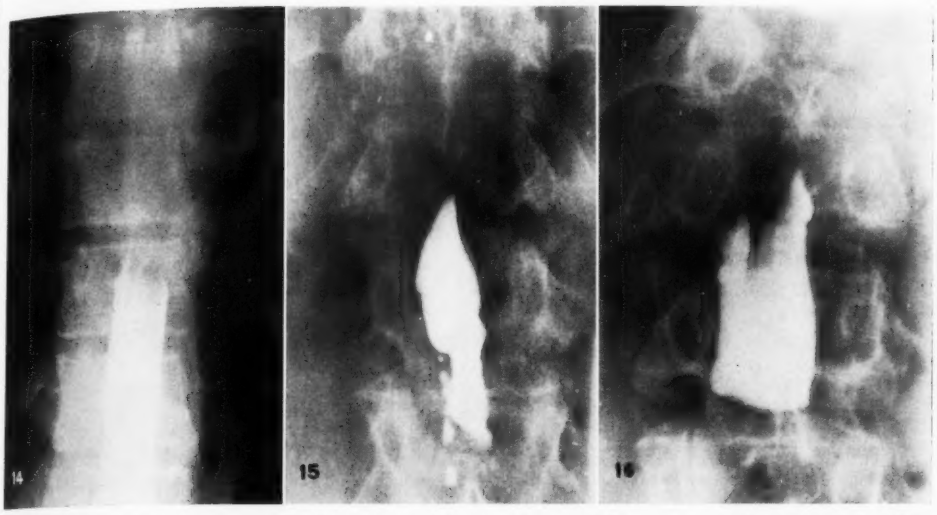

Fig. 14. Extradural neurofibroma, T9, in a 30-year-old man. Interpedicle measurement increased and pedicles compressed at T8. Serrated transverse block. Marked displacement of subarachnoid space from right pedicle T9.

Fig. 15. Extradural lymphosarcoma, T11-L1, in a 63-year-old woman. Osteoblastic change at T11. Tapered block with marked separation of subarachnoid space from pedicles on each side.

Fig. 16. Extradural leukemia, T12, in a 53-year-old woman. Oblique slightly serrated block with no cord displacement. The left subarachnoid space is narrowed and considerably separated from the left pedicles of T12 and L1.

the displacement is in a lateral direction, it is usually evident on the frontal myelogram. The importance of the lateral view is evident, however, in those cases in which there is dorsal or ventral deviation of the cord without lateral displacement. The determination of cord displacement is obviously of value only above LI-L2.

C. Width of the Subarachnoid Space: Extradural masses compress the adjacent subarachnoid space and, if of sufficient size, that on the opposite side as well. The position of the tumor will determine whether this compression is seen in the frontal or lateral projection. It is manifested by a tapering deformity of the opaque column. The nerve root recesses may be compressed, deformed, or obliterated.

D. Contour of the Opaque Column with Complete Block: Extradural mass lesions with complete block on myelography most frequently show a transverse serrated edge at the level of the obstruction. This contour is probably explained by the compression and approximation of the dura, subarachnoid fluid, and spinal cord (or cauda equina). In eccentric tumors, the unyielding wall of the contralateral bony spinal canal is a contributing factor. On the other hand, annular concentric extradural lesions probably contribute to this type of deformity at the level of the block.

PITFALLS OF MYELOGRAPHY

Although plain films and myelograms usually localize the level of the neoplasm in the spinal canal, one should be alerted to certain pitfalls of myelography. In patients in whom complete block is suspected, a smaller volume of opaque medium may be used at the demand of the neurosurgeon. There should be sufficient opaque material to permit complete filling of the subarachnoid space for about the height of one vertebral body. In all instances frontal and lateral projections should be obtained. The omission of the lateral projection may prevent the visualization of the

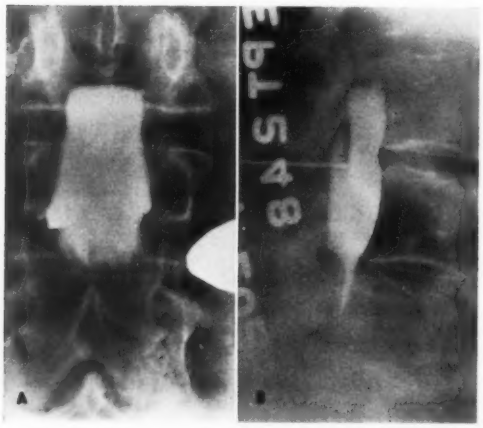

Fig. 17. Extradural lymphoblastoma, L3-L4, in a 64-year-old man. A. Serrated transverse block. B. Mass compressing dorsal aspect of opaque column, with increased distance of bony spinal canal to subarachnoid space.

"cupping" defect so characteristically found in intradural lesions. At times, for precise visualization of the myelographic deformity, it is probably necessary to include oblique projections. Dorsal defects due to intradural or extradural lesions may go undetected in the prone position if the dorsal subarachnoid space is incompletely visualized. In such cases, it may be advisable to examine the patient in the supine position with both frontal and lateral views.

Edema of the spinal cord in relationship to an adjacent neoplasm may so alter the myelographic deformity that it simulates an intramedullary space-occupying lesion. In some instances, intraspinal neoplasms are associated with enlarged vessels in the subarachnoid space. If these occur in the region of the block, they may be mistaken for the "cup" defect of an intradural extramedullary tumor.

Variations in the length and contour of the caudal sac must be appreciated before a diagnosis is made of an abnormality in this region, particularly of the extradural type. Any asymmetry or irregularity in the contour of the caudal sac should arouse suspicion; a conical tapering requires careful evaluation. In such cases, review of the plain roentgenograms of the lumbosacral spine will frequently disclose bony abnormalities as encountered in an extradural type of neoplasm. Any suspicious areas can be studied further by additional roentgenograms, including laminagrams, of the bony structures.

In patients past middle age, indentations are not infrequently encountered on the ventral aspect of the opaque myelogram in translateral projections. These represent the so-called "ridging" syndrome and

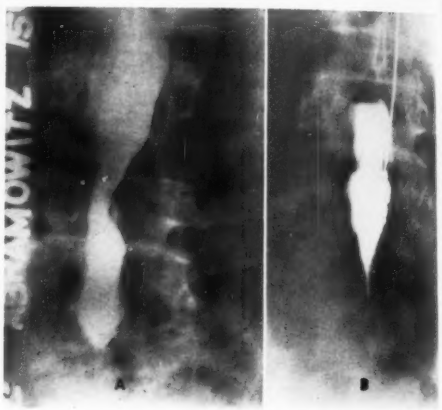

Fig. 18. Extradural metastatic bronchogenic carcinoma in a 58-year-old man, with incomplete obstruction at L3 and complete block at S1. Destruction of the upper sacrum and left pedicle of L3. A. Left eccentric narrowing of opaque column at L3 with marked displacement of the subarachnoid space from the left pedicle. B. Marked conical narrowing of the caudal sac due to concentric extradural tumor.

occur most frequently in the cervical and lumbar spine. Characteristically, the indentation is present opposite the level of the disk cartilage and is associated with spondylosis deformans and degenerative disk disease. Single or multiple indentations of this type must not be mistaken for extradural neoplasms.

SUMMARY AND CONCLUSIONS

1. The plain-film and myelographic findings in a series of 87 cases of extramedullary intradural and extradural neoplasms are presented.

2. An evaluation of the myelographic

changes in these two categories, with particular reference to the position of the spinal cord and the appearance of the subarachnoid space, indicates that it is usually possible to make a correct localization of an intraspinal tumor.

3. Brief discussions of myelographic technics and anatomy are presented.

4. The myelographic patterns in intradural extramedullary and extradural neoplasms are evaluated.

5. The literature dealing with this subject is reviewed.

210th St. and Bainbridge Ave.
New York 67, N. Y.

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SUMMARIO IN INTERLINGUA

Le Diagnose Differential de Tumores del Canal Spinal de Sito Intradural (Extramedullari) e Extradural

Iste communication concerne le location differential de massas extra- e intradural. Es describite brevemente le anatomia del columna vertebral e le technica de myelographia a usar. Le litteratura ab 1938 ad hodie es revistate. Un serie de 51 casos de tumores extradural e de 36 casos de tumores intradural extramedullari esseva re-examinate. In roentgenogrammas conventional del 87 casos, massas de tissu molle esseva visibile in 6 del casos de lesiones extradural e in nulle del casos de lesiones intradural. Esseva etiam constatate un plus alte frequentia de affectiones de osso in le gruppo de tumores extradural.

Certe typos myelographic emergeva.

Tumores intradural: (1) Un tumor intradural pote displaciar le medulla spinal contralateralmente. (2) Le columna opac pote esser displaciate verso le canal ossee, con allargamento del opacificate spatio subarachnoide circum le massa e compression del spatio subarachnoide contralateral. (3) Un defecto radiolucente es producite in le columna opac in le canal infra le nivello del medulla. Iste defecto es eccentric in su position e es attachate al portion circumferential del columna opac. Un massa sessile o pedunculate es a vices identificate. (4) In caso de bloco complete del myelogramma, un deformitate del typo designate como "cuppiforme" (reflectente le precise loco del anormalitate) es delineate per le medio in le aspecto caudal del massa polypoide (in myelographia effectuate per le via lumbar).

Tumores extradural: (1) Le columna opac es displaciate ab le aspecto interne del canal spinal e in particular ab le aspecto interne del pediculo. (2) Un eccentric lesion extradural de sufficiente dimensiones displacia le medulla spinal a distantiation ab le massa, sed lesiones concentric tende a fixar le medulla in su position central. (3) Le massa comprime le adjacente spatio subarachnoide; si illo es sufficientemente grande, etiam le correspondente spatio contralateral. Isto es manifeste in un deformitate coniforme del columna opac. (4) In caso de bloco complete, un serrate margine transverse al nivello del obstruction se face visibile.

Es discutite certe facilemente occurente errores in le myelographia.

Pneumatosis Intestinalis: A New Concept

WALTER S. KEYTING, M.D., ROBERT R. McCARVER, M.D., JOSEPH L. KOVARIK, M.D., and ALVIN L. DAYWITT, M.D.

OUR INTEREST in the subject of pneumatosis intestinalis and, in particular, its etiology, was stimulated by the occurrence of 3 cases in our hospital within one month. The common feature in these cases was severe pulmonary disease in exacerbation and lack of gastrointestinal complaints or demonstrable gastrointestinal involvement prior to the onset of the pneumatosis. This suggested that pneumatosis intestinalis in a significant number of cases might occur as a result of air in the lung becoming interstitial from alveolar rupture, subsequently passing to the mediastinum and thence to the retroperitoneal area, and then dissecting along the vascular supply of the viscera. This seemed the more probable in that the distribution of the pneumatosis in our cases seemed to follow the pattern of vascular supply. Our experimental work has been directed toward proving or disproving this concept.

Very soon after we started laboratory investigation, impetus to our study was given by a report by Doub and Shea (1) of 16 cases of pneumatosis intestinalis, of which 15 were associated with asthma and 1 with pulmonary fibrosis. A majority of their cases occurred in the left colon, while our small series involved predominantly the right and transverse colon.

HISTORICAL

Probably the key paper on this subject is that of Macklin (2), published in 1939. This excellent treatise does not even mention "pneumatosis intestinalis" but does report the experimental production of "emphysema" of the mediastinum, neck, axilla, and pericardium, pneumothorax, and air in the retroperitoneal space as a result of alveolar ectasia and rupture. We are concerned with the latter and propose

Fig. 1. Lateral view of pig showing retroperitoneal air about the sigmoid.

to show that the presence of retroperitoneal air is at least a potential for pneumatosis intestinalis. Macklin clearly demonstrated that air from alveolar rupture dissects along pulmonary vessels to the lung root and mediastinum and then takes divergent routes, as mentioned above.

Koss (3) summarized the literature on pneumatosis intestinalis up to 1952, including 213 reported cases. Fifty-eight per cent were explained on the mechanical basis of duodenal or pyloric obstruction (perforation assumed). A few other cases were attributed to sigmoidoscopy or biopsy of the sigmoid, or appendiceal disease. This left approximately 40 per cent in the "primary" category, *i.e.*, etiology unknown.

[1] From the Departments of Radiology and Surgery, Veterans Administration Hospital, Denver, Colo. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

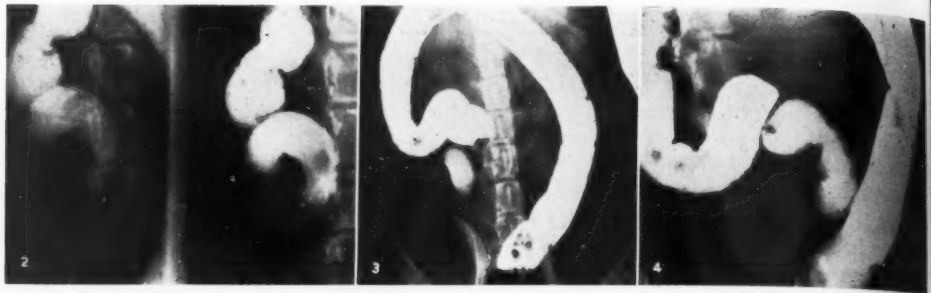
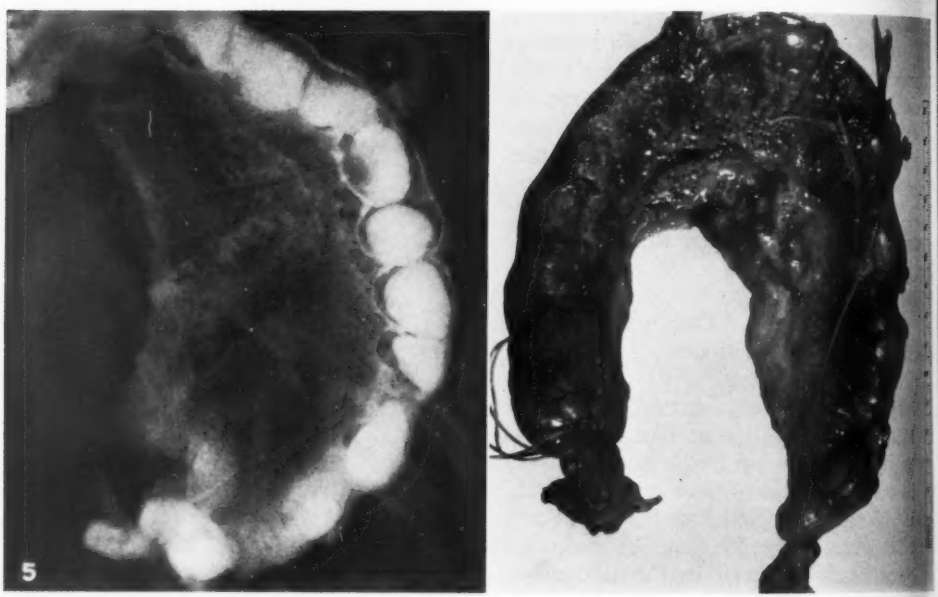


Fig. 2–4. Experimental studies on a dog. Fig. 2 shows "linear" pneumatosis of the cecum. Figs. 3 and 4 show "linear" and "cystoides" pneumatosis.



Figs. 5 and 6. Sigmoid colon of cadaver showing subserosal and intramesenteric air from injection along the inferior mesenteric artery.

Theories of the etiology of pneumatosis intestinalis have basically been of three types: mechanical, neoplastic, and bacterial. Only the mechanical theory has been supported by documented proof. Multiple articles, reporting 1 to 7 cases and reviewing the literature, lean toward the mechanical theory, when they lean at all. It is interesting to note that the report of 7 cases by Mujahed and Evans (4) included 5 with pulmonary disease.

METHODS OF INVESTIGATION

The dog, the pig, and the unembalmed cadaver were used for our experimental investigations. Only 1 pig was studied, a dead specimen, immediately following hepatectomy for another research project. In this animal, the posterior mediastinal structures, as well as the retroperitoneal space, were intact. A polyethylene catheter was placed in the supporting tissue of the thoracic aorta, after which air was injected by means of a 50-c.c. syringe and 3-way stopcock. The air passed with relative ease and minimal (or no) resistance to the syringe plunger down the outside of the aorta until its course was lost at the

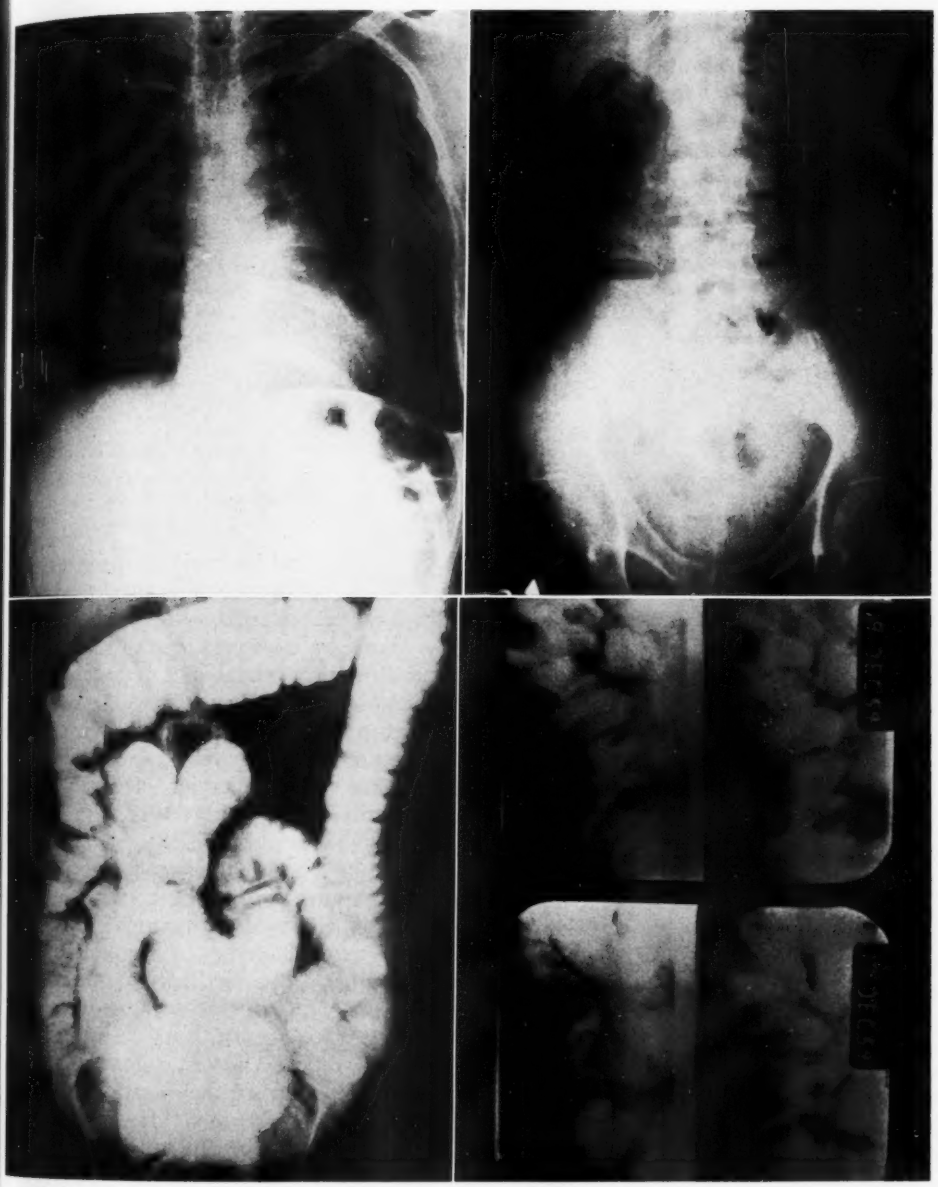


Fig. 7. Case I. Vague abdominal symptoms led to abdominal examination. Diagnosis of pneumatosis was made from the plain film prior to a barium-enema study. Note "highlighting" of right colon, cyst on cyst. The patient was on steroids and medication for tuberculosis and had a hard, persistent cough.

diaphragm. However, air was then seen to pass subserosally around the lower esophagus and subserosally over the anterior aspect of the stomach until it escaped through a rent in the peritoneum incident to the hepatectomy. Inspection of the abdominal viscera revealed a large collection of retroperitoneal air in the pelvis, and a gross subserosal pneumatosis of the sigmoid colon, which literally floated in a capsule of air extending 20 cm. of its length (Fig. 1).

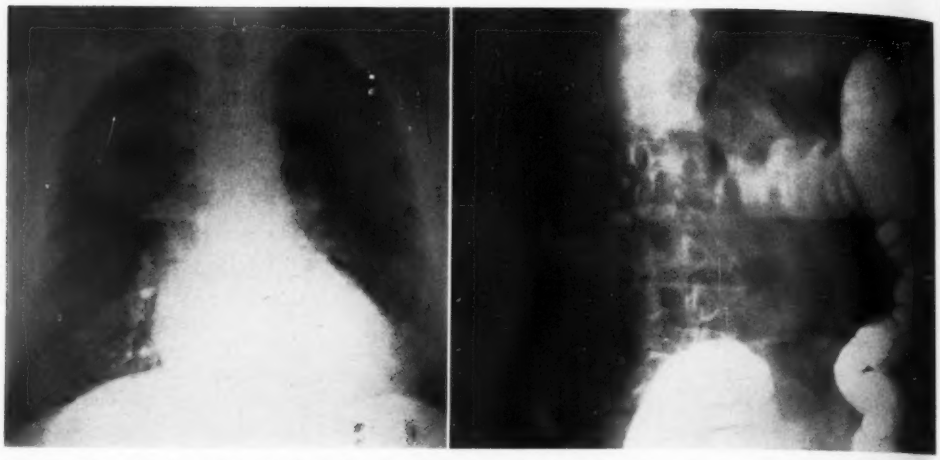
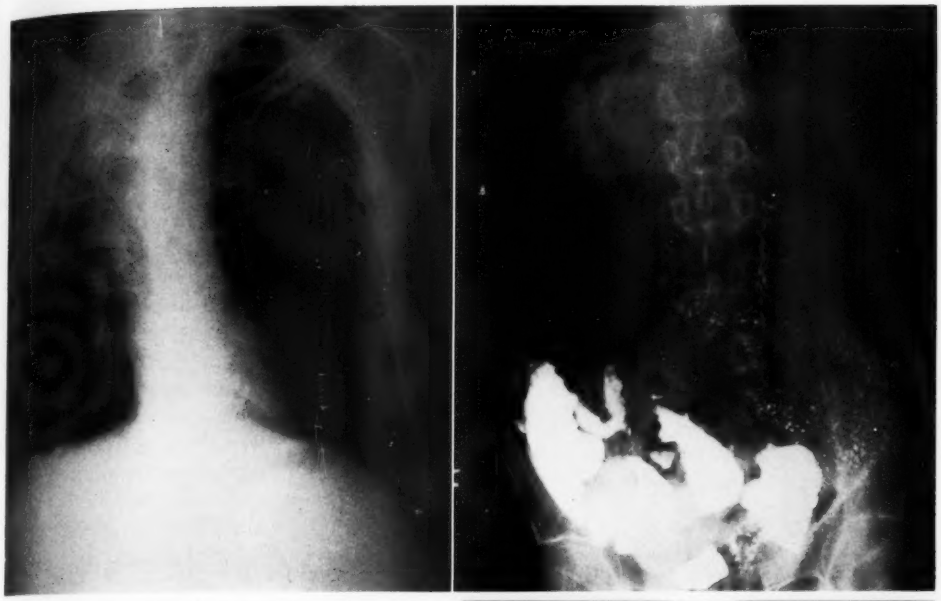


Fig. 8. Case II, in a chronic alcoholic with cirrhosis. Cough and dyspnea for two months; cardiac enlargement and early failure. *D. pneumoniae* was cultured from sputum. Diarrhea led to a barium-enema study.

Work with dogs was in every instance with the living animal. Efforts directed toward producing a pneumatosis by injection of the retroperitoneal space directly through an open abdominal incision were unsuccessful. In these instances, only a small amount of air (100 to 150 c.c.) was used for fear of rupturing the rather delicate posterior peritoneum, and no pneumatosis was detected on subsequent studies. A single animal in which an effort was made to introduce a catheter into the superior mediastinum through the suprasternal notch promptly died from cardiac arrest. Several animals expired within two to six hours after a polyethylene tube was secured in the left main-stem bronchus with the other end buried in the mediastinum. Death was due to bilateral pneumothorax and pulmonary vein tamponade. Successful studies on the dog followed thoracotomy, with subsequent mediastinal injection through a needle passed into the mediastinum at the root of the left lung. In 1 such case, air filled the superior mediastinum and the animal died twelve hours later with no evidence of a pneumatosis. In the 3 other dogs similarly injected, air was seen to pass easily down the supporting tissue about the aorta until it was lost from view below the diaphragm. Twenty-four hours later, on plain films and by barium-enema examination, a pneumatosis was demonstrated in 2 of these animals (Figs. 2–4).

Work on cadavers was directed toward proving that air would travel along the route of vascular supply of the colon and produce a pneumatosis. The inferior mesenteric artery was chosen for injection because of its easier accessibility. A polyethylene catheter and a 50-c.c. syringe, as previously described, were again used. Through a small incision in the posterior peritoneum, the inferior mesenteric artery was identified at its point of origin from the aorta. The tip of the catheter was placed in the supporting tissue of this vessel and air was injected. Subsequently, air was seen to follow the course of the vessels to the wall of the left colon. From this point, it climbed subserosally over the colon and then dissected freely, proximally and distally, over the colon in the same plane, producing multiple small cysts, many of which became confluent (Figs. 5 and 6). It is of interest that the air reached the wall of the colon *via* one vessel, or at most two, and then seemed to follow a route of least resistance, in that it continued to flow subserosally, distally and proximally, over the colon *via* these one or two vessels. It did not continue to advance over other partially established



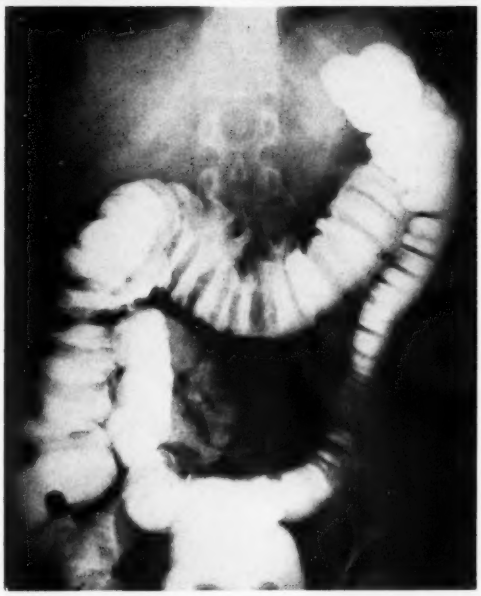


Fig. 9. Case III. Chronic, active, far-advanced tuberculosis, with severe cough for four weeks before development of pneumatosis. *D. pneumoniae* cultured. No abdominal complaints. Note "linear" pneumatosis at hepatic flexure.

vascular routes. This sequence of events would seem to indicate that, of the many arterial branch routes available for air to find its way to the bowel wall, it is necessary only that it reach the bowel by one branch for a sizable pneumatosis to ensue.

DISCUSSION

Following a review of the literature on pneumatosis intestinalis, and considering the results of our experimental work, we contend that the concept of primary and secondary etiology of pneumatosis intestinalis should be abandoned and that all cases fall into the secondary group. In other words, a cause can be established if a cause is sought, and the pneumatosis is invariably secondary to other conditions. The subject will be further clarified when the neoplastic and bacterial theories are properly relegated to the background.

It is proposed that the mechanical theory of production of pneumatosis intestinalis will explain all cases, and that three major mechanisms are responsible: (*a*) *obstruction*, which implies perforation secondary to duodenal or pyloric ulcer, volvulus, tumor, and less frequently occurring conditions; (*b*) *trauma*, resulting from sigmoidoscopy, and/or biopsy, pneumoperitoneum, and presacral air studies; (*c*) *development secondary to pulmonary disease* with severe cough, resulting in pneumomediastinum and air dissection downward,

Fig. 10. Case IV. Chronic pulmonary tuberculosis with superimposed pneumonia and cough. Vague abdominal complaints led to barium-enema examination.

retroperitoneally, and then along a vascular route to the bowel wall.

We would further propose that "pneumatosis intestinalis" be considered as a generic term and that the designation "pneumatosis cystoides intestinalis" be abandoned. The disease manifests itself variously, (*a*) as large cystic accumulations of air displacing the bowel lumen; (*b*) in a linear fashion along the visceral wall, without significant displacement of the bowel lumen; and (*c*) as a mesenteric distribution of air. We feel that these three manifestations are all part and parcel of the same process and that the manner in which the disease presents is but a matter of degree of pressure gradient acting through a variable length of time and probably modified by bowel activity and strength of fascial planes.

Analyses have been made of the "air" content of pneumatosis blebs. These show a relatively high nitrogen content as compared to the oxygen content. We propose that the analyses are relative; *i.e.*, oxygen

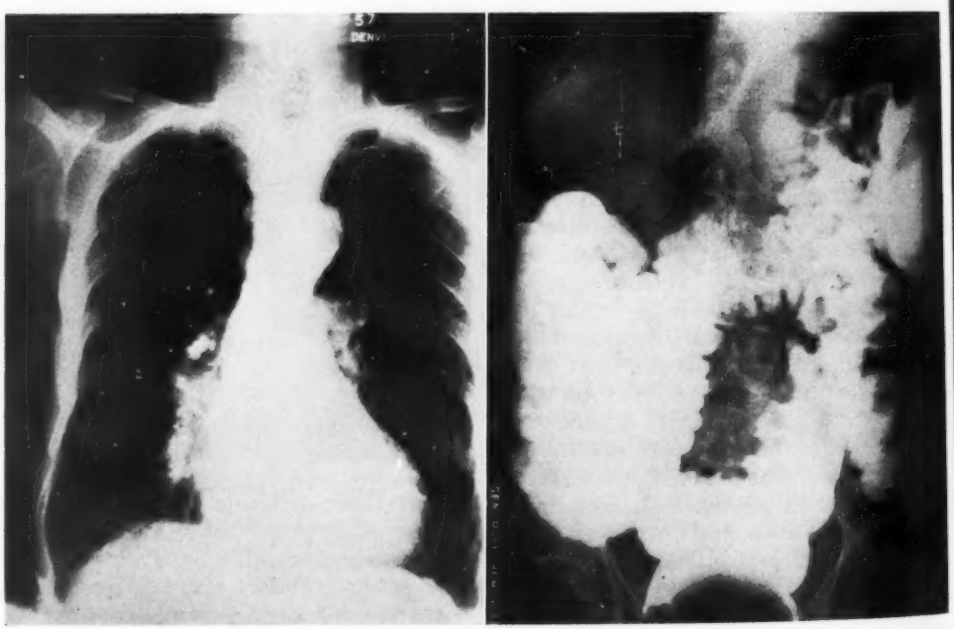
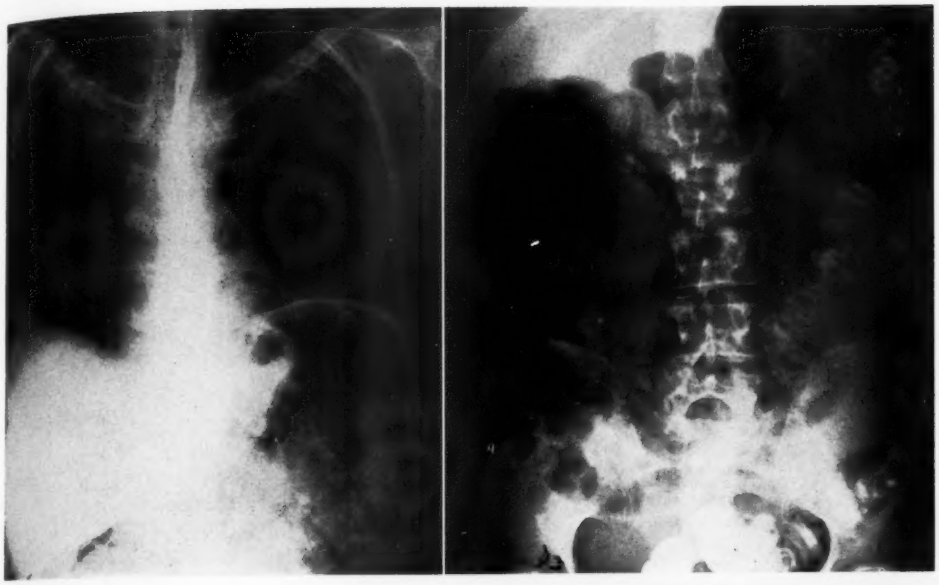


Fig. 11. Case V. Pulmonary emphysema and fibrosis. Several days of hard coughing preceded onset of vague abdominal complaints that led to a barium-enema examination. Note "linear" pneumatosis at splenic flexure.



is first absorbed and, if the analysis were made early, it would approximate that of air; in later analyses nitrogen would predominate.

The cases shown here demonstrate a distribution of pneumatosis clearly related to the vascular pattern of the bowel segments involved. Cases I to IV (Figs. 7-10) can be explained by air dissection along the superior mesenteric artery and to the bowel wall *via* the ileocolic and middle colic branches. In Case V (Fig. 11) the distribution follows the inferior mesenteric artery. Case VI, in which a continuing blast of air persisted over several months, shows a pattern of dissection of all major abdominal vessels, celiac axis, and both mesenterics (Fig. 12). Case VII (Fig. 13), a sigmoid volvulus, is an example of pure obstruction with mucosal ulceration allowing a leak of air subserosally. Note that there are no "cysts" and that air is strictly linear in distribution. This case was proved surgically and obviously no vascular pattern can be identified. It has previously been well documented that most cases secondary to duodenal and pyloric disease show dissection into the small bowel only, and this presumably is due to perforation at or in communication with the root of the mesentery.

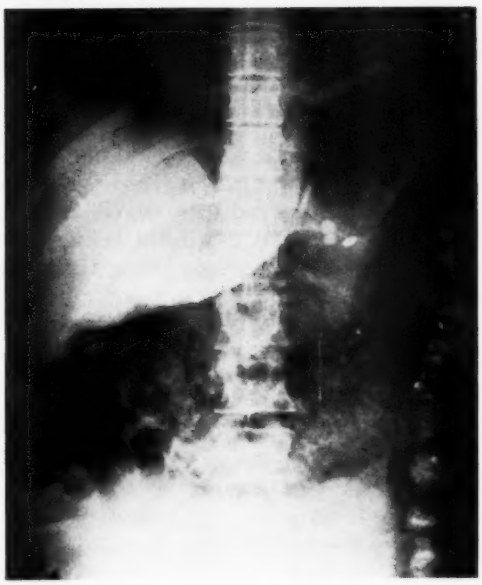


Fig. 12. Case VI. Chronic tuberculosis with miliary reactivation and severe cough; abdominal distention. Diagnosis of pneumatosis first made from chest film. Appearance suggests dissection of air along the celiac axis and mesenteric vessels. Note "linear" pneumatosis in stomach and colon and radial distribution of air in mesentery.

Fig. 13. Case VII. Chronic partial obstruction with volvulus repeatedly demonstrated for eight years. At operation, a small mucosal ulceration was found at "twist" at splenic flexure, with obvious subserosal emphysema. Chest film normal. Note "linear" pneumatosis.

CLINICAL OBSERVATIONS

It is felt that the development of vague abdominal symptoms in anyone with chronic pulmonary disease should arouse suspicion of pneumatosis intestinalis. The diagnosis can be strongly suspected from a plain abdominal film and confirmed, if necessary, by barium-enema examination. When pneumatosis is secondary to pulmonary disease, it is not a surgical condition, even when pneumoperitoneum results. Differential diagnostic considerations include polyposis coli, pseudopolyposis coli, and phlegmonous gastritis.

It has been pointed out that most infantile pneumatosis intestinalis is submucosal instead of subserosal, as in the adult. The diarrhea and partial obstruction in the infant can cause severe electrolytic imbalance, with a much graver prognosis, especially if unrecognized. It is also felt that, in the majority of cases, infantile pneumatosis intestinalis is secondary to obstruction within the abdomen rather than "thoracic." Investigation into the possible association of pneumatosis intestinalis and cystic fibrosis seems to be in order.

Recently it has been suggested that the use of steroids may play an associated etiological role in the development of pneumatosis. Originally we felt strongly concerning this point but we now believe that pulmonary pneumatosis occurs in those chest conditions in which steroids are most likely to be used as part of the treatment; namely, asthma, pulmonary tuberculosis, and pulmonary fibrosis. The complications of the primary disease rather than steroid medication, *per se*, better explain the pneumatosis. We would not, however, deny that steroids may be a contributing factor.

SUMMARY AND CONCLUSIONS

1. Seven additional cases of pneumatosis intestinalis are submitted for the record. Six of these were clearly associated with moderate to severe pulmonary disease.

2. Experimental studies demonstrated a route by which pneumatosis intestinalis

may develop from pulmonary disease which leads to alveolar rupture.

3. The conclusion is reached that most, if not all, cases of so-called "primary pneumatosis" can be explained on the basis of pulmonary disease, associated with harsh cough, alveolar rupture, pneumomediastinum, and retroperitoneal air advancing along vascular routes to the wall of the bowel.

4. Gastrointestinal obstruction and trauma are recognized as mechanical causes explaining the majority of cases of pneumatosis intestinalis.

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1055 Clermont Street
Denver 20, Colo.

SUMMARIO IN INTERLINGUA

Pneumatosis Intestinal: Un Nove Concepto

Super le base del litteratura e de su proprie observationes experimental e clinic, le autor propone que omne casos de pneumatosis intestinal pote esser explicate a bases mechanic. Le tres mechanismos interessate es (1) obstruction, (2) trauma, e (3) disveloppamento secundari a morbo pulmonar con tusse sever, resultante in rupturas alveolar, pneumonomediastino, dispersion retroperitonee de aere, e progresso de aere al longo de vias vascular verso le pariete intestinal. Le majoritate, si non le totalitate, del si-appellate casos primari de pneumatosis intestinal pote esser explicate a base del tertie mechanismo.

Es reportate septe casos de pneumatosis intestinal. Sex esseva nettemente associate con sever morbo pulmonar.

Vertebral Arteriography by Retrograde Injection of the Right Common Carotid Artery[1]

GEORGE T. TINDALL, M.D., and HORACE B. CUPP, JR., M.D.

THIS REPORT describes a simple method for obtaining vertebral arteriograms during the course of carotid arteriography. It is a modification of a previously described "open" technic in which filling of the vertebral arterial system is accomplished by retrograde injection of contrast media into the right common carotid artery (1). The results of the present study show that vertebral arteriograms of diagnostic quality can be obtained in 70 per cent of the cases investigated.

METHOD

Vertebral arteriography by retrograde injection of the right common carotid artery is performed as follows: The patient is placed on the x-ray table, in a supine position, and the neck is hyperextended by folded sheets placed beneath the shoulders. The skin is prepared with a suitable antiseptic (Merthiolate) and a local anesthetic (1 per cent procaine or 1 per cent lidocaine) is injected into the skin and deeper cervical tissues about the common carotid artery. The position of the arteriographer is at the head of the table on the patient's left. A 17-gauge needle[2] is inserted and threaded into the right common carotid artery with the point directed toward the heart. The design of the tip is such that it can be threaded easily down the artery. Connected to the needle is a plastic tube[3] filled with saline containing heparin.[4] The position of the needle in the neck and its relation to the bifurcation of the artery are shown in Figures 1 and 2.

The injections of contrast medium are made manually, as rapidly as possible, in a retrograde direction into the right common carotid artery while an assistant maintains percutaneous compression of the artery distal to the point of puncture. A volume of 20 c.c. of 50 per cent Hypaque (sodium diatrizoate) is used for each injection. The radiographic exposure is called as the plunger strikes the bottom of the syringe. The medium flows down into the right subclavian artery and thence into the right vertebral artery as well as the other branches of the subclavian artery. A blood-pressure cuff high about the right arm is inflated to above systolic blood pressure during the injection to prevent flow of the contrast material into the brachial artery.

This technic of vertebral arteriography was evaluated in a total of 60 patients with a presumptive clinical diagnosis of brain tumor, subarachnoid hemorrhage, or carotid thrombosis. Patients with marked depression of consciousness or striking neurological deficit were not included.

The contrast agent used throughout the study was Hypaque. During the early phase of the study, both 50 per cent and 70 per cent Hypaque, in volumes ranging from 10 to 30 c.c., were used, the 70 per cent concentration being obtained by mixing equal quantities of 50 and 90 per cent preparations. In the majority of cases, 20 c.c. of 50 per cent Hypaque per injection was used to obtain an indirect vertebral arteriogram.

Carotid arteriography was performed in

[1] From the Department of Surgery, Division of Neurosurgery, Duke University Medical Center and Durham Veterans Administration Hospital, Durham, N. C. Presented at the Thirteenth Annual Meeting of the Southern Neurological Society, San Antonio, Texas, Feb. 2-4, 1961. Accepted for publication in October 1960.

This study was supported by research grants from the National Paraplegic Foundation and the United Medical Research Foundation.

[2] 17-gauge 3-inch thin wall Touhy needle with a Huber tip. No. T4 66LNRH, Becton, Dickinson & Co., Rutherford, N. J.

[3] Abbott Venotube, Abbott Laboratories.

[4] 50 mg. heparin per 1,000 c.c. isotonic saline.

Fig. 1. Position of needle and attached tube in a retrograde direction in the right common carotid artery. The needle is inserted into the artery below the bifurcation.

Fig. 2. Lateral roentgenogram of head and neck during injection of 50 per cent Hypaque to show relationship of needle to right common carotid artery and its bifurcation. There is segmental narrowing of both the internal and external carotid arteries.

each patient even though the needle was placed in a retrograde direction. A volume of 10 c.c. of 50 per cent Hypaque was used for each injection. The radiographic exposure was made approximately one-half second after the plunger struck the bottom of the syringe. These injections were made with slightly less force than for the retrograde vertebral arteriogram, and the brachial and distal carotid arteries were not compressed.

Anteroposterior roentgenograms of the upper chest and neck were made in 14 of the 60 patients during the retrograde injection of contrast medium into the common carotid artery. The right common carotid artery was injected in 8 patients and the left common carotid artery in 6. A single injection of 20 to 25 c.c. of 70 per cent Hypaque was made while compression of both the common carotid artery distal to the point of puncture and the ipsilateral brachial artery was being applied. The retrograde injections into the left common carotid artery were carried out in an effort to fill the left vertebral artery.

The quality of the vertebral arteriograms obtained by retrograde injection was evaluated according to the following classification: (*a*) no filling; (*b*) poor filling, not useful diagnostically; (*c*) fair, useful; (*d*) good. In the poor filling group, part of the intracranial portion of the right vertebral or basilar artery or both could be faintly visualized. Occasionally, the proximal portion of one or both posterior cerebral arteries could be seen. These films were not considered diagnostic. With *fair, useful filling*, the right vertebral and basilar, and one or both posterior cerebral arteries could be seen, but the degree of contrast

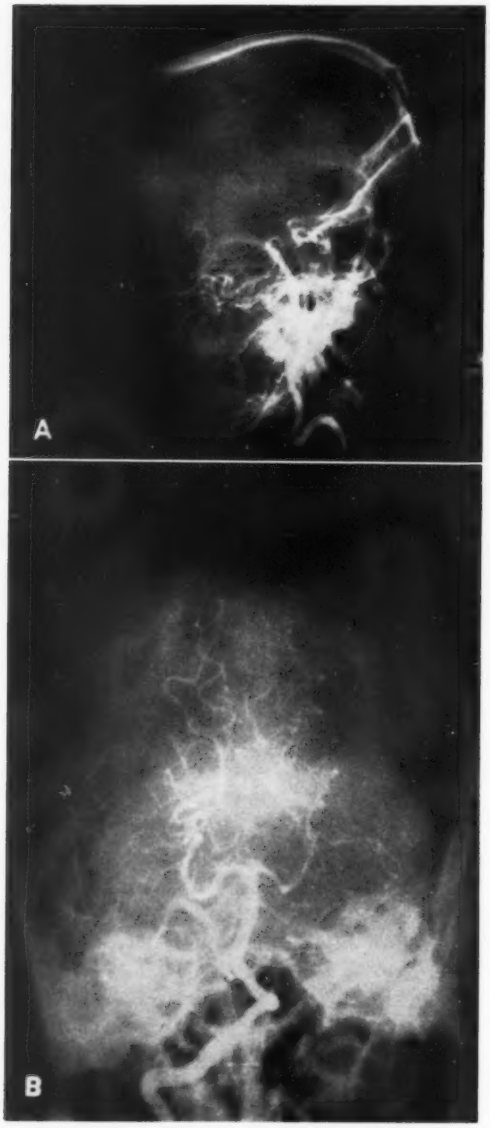

Fig. 3. Lateral (A) and anteroposterior (B) roentgenograms illustrating examples of good filling of the vertebral arterial system following retrograde injection of 50 per cent Hypaque into the right common carotid artery.

was light. However, displacement of the basilar artery or the presence of an aneurysm or vascular anomaly could be detected. *Good filling* meant good visualization of the right vertebral, basilar, and both posterior cerebral arteries (Fig. 3).

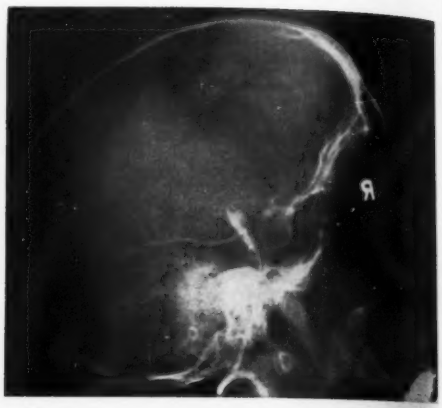

Fig. 4. Retrograde vertebral arteriogram showing large aneurysm of the basilar artery. A second aneurysm is also seen on the right posterior communicating artery near its junction with the internal carotid artery.

In the majority of cases, the right posterior communicating artery and intracranial portion of the right internal carotid artery could be visualized.

RESULTS

A total of 125 retrograde carotid injections were made in the group of 60 patients. The quality of the vertebral arteriograms resulting from these injections was as follows: Good, 39 instances; fair but useful, 46; poor and not useful for diagnostic purposes, 20; no intracranial filling of the vertebral arterial system, 20. A vertebral arteriogram of diagnostic quality was obtained in 42, or 70 per cent, of the 60 patients in this series.

Incomplete compression of the distal carotid artery or improper timing was responsible for inadequate visualization of the vertebral arterial system in the majority of cases. Compression of the distal artery was incomplete in 19 instances, thus allowing the contrast medium to flow into the distal carotid system.

There were 4 patients in this series with basilar artery aneurysms and 2 with arteriovenous malformations located mainly in the posterior fossa (Figs. 4 and 5). In all but one case, the diagnosis was established by retrograde vertebral arteriography.

The right posterior communicating artery was visualized in the majority of patients in whom a vertebral arteriogram of good quality was obtained. In these instances, filling of the internal carotid system through the posterior communicating artery was obtained.

Fig. 5. Retrograde vertebral arteriogram showing arteriovenous malformation in the region of the vein of Galen.

There was good visualization of the proximal portion of the right common carotid, as well as the right subclavian artery and its branches, in all 8 cases in which anteroposterior roentgenograms of the upper chest and neck were made during retrograde injection into the right common carotid artery (Fig. 6). The left vertebral artery was not visualized in any of the 6 patients in whom retrograde injections were made into the left common carotid artery, with maintenance of distal carotid and left brachial artery occlusion. Anteroposterior roentgenograms of the neck and chest during retrograde injection of the left common carotid artery showed the contrast medium to flow into and outline the thoracic aorta. In these cases, the other major branches of the aorta such as the left subclavian artery were not visualized. The carotid arteriograms obtained with the needle placed in a retrograde direction in the right common carotid artery were comparable to those obtained when the needle is directed in the conventional or cephalic direction with but 4 exceptions.

Fig. 6. Anteroposterior roentgenogram of the neck and upper chest during injection of 70 per cent Hypaque in a retrograde direction through the right common carotid artery, demonstrating the degree of filling of the right subclavian artery and its branches. The right vertebral artery is indicated by the arrow. The distal carotid and right brachial arteries were compressed during injection.

DISCUSSION

Indirect vertebral arteriography by retrograde injection of the common carotid artery was first described by Elvidge in 1938 (1). He exposed the common carotid artery and inserted the needle with the point directed toward the heart. The distal common carotid and ipsilateral axillary arteries were compressed during the injection. Ameli (2) obtained satisfactory vertebral arteriograms in more than 20 cases by retrograde injection of contrast medium (20 c.c. of 50 per cent diodone for each injection) into the right common carotid artery. During the injection, the distal right common carotid and right subclavian arteries were occluded, the latter by digital pressure against the first rib. Schaerer (3), using essentially the same technic except that the right brachial rather than the subclavian artery was occluded, obtained

excellent filling of the vertebral system in 44 out of 52 instances. The principal objection to these methods is the fact that they are "open," *i.e.*, the right common carotid artery was exposed surgically prior to carrying out arteriography. Although our method is similar in principle, it is simpler in that it is done by percutaneous puncture rather than by the open technic. Ecker (4) describes a percutaneous method in which filling of the vertebral artery is obtained by injection of the right common carotid artery. However, compression of the carotid distal to the needle tip is uncertain, since the needle is placed in the conventional or cephalic direction. Also, firm compression over the tip of the arterial needle might damage the wall of the artery or dislodge the needle from the lumen of the vessel.

One drawback of the percutaneous retrograde method is that complete occlusion of the distal common carotid artery is not always assured. There were 19 out of 125 instances in the present series in which compression of the right common carotid artery above the injection site was inadequate, for the most part in patients who were restless and uncooperative. Because of this possibility, it is felt that the same percentage of contrast medium used for carotid arteriograms should be used for the retrograde vertebral arteriogram.

The vertebral arteriograms obtained by the direct or catheter methods are superior in degree of contrast, and the incidence of filling is higher, than with retrograde carotid injection. Radner (5) reported failure in only 1 out of 100 cases investigated with the perfected catheter method. A failure means that the catheter could not be passed up either side. Although it is not specifically stated, it is assumed that diagnostic films were obtained in those patients in whom catheterization was successful. Lindgren (6) employed the direct percutaneous technic in 60 cases. In about two-thirds of the cases percutaneous puncture of the vertebral artery was possible. Sjögren (7) reported failure to perform percutaneous vertebral arteriography in only 2 of 150 cases in which the procedure was attempted. The degree of filling of the intracranial branches in 10 cases was not satisfactory. Sugar, Holden, and Powell (8) failed to fill the vertebral artery in 2 out of "more than 20 successive deliberate vertebral angiograms." Freshwater (9) obtained satisfactory vertebral arteriograms in 51 of 68 patients studied. Sjögren performed direct puncture of the vertebral artery under local anesthesia; whereas Freshwater and Sugar, Holden, and Powell used general anesthesia. It has been our experience that general anesthesia is necessary in order consistently to obtain vertebral arteriograms of good to excellent quality with direct percutaneous method. The two chief advantages of the retrograde method are that it can be accomplished under local anesthesia and it avoids the necessity for puncturing the vertebral artery. The principal use of the retrograde method in our clinic has been in patients with subarachnoid hemorrhage. In these cases, a complete survey of the intracranial arterial circulation can be accomplished in one session, through bilateral carotid artery punctures.

Because of the manner in which the arterial needle is inserted, the technic described here is worthy of consideration in patients with varying degrees of thrombosis of the internal carotid artery in the neck. Retrograde insertion of the arterial needle below the bifurcation of the common carotid artery in these cases avoids the risk of threading the tip of the needle into the involved portion of the vessel. The possibility of threading the needle into the external carotid artery and gaining the false impression of internal carotid thrombosis is also eliminated.

The fact that the right subclavian, proximal portions of the right and left common carotids, and right vertebral arteries can be visualized with this technic makes it desirable in patients in whom arteriosclerotic involvement of the vessels in these locations is suspected. Because

with retrograde injection into the left common carotid artery, most of the contrast material flows into the aorta, the one "blind spot" in this technic is the failure to visualize the left vertebral artery.

SUMMARY

Vertebral arteriography was performed by retrograde injection of contrast medium into the right common carotid artery, percutaneously, while the distal common carotid and right brachial arteries were compressed.

A vertebral arteriogram of diagnostic quality was obtained in 42, or 70 per cent, of the 60 patients in this series.

Retrograde injection of the right common carotid artery is useful in demonstrating the right subclavian as well as the proximal portions of the right and left common carotid and right vertebral arteries.

Retrograde insertion of the arterial needle into the common carotid artery avoids the risk of threading the tip of the needle into involved segments of vessels in patients with thrombosis of the internal carotid artery in the neck.

Department of Surgery
Duke University Medical Center
Durham, N. C.

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SUMMARIO IN INTERLINGUA

Arteriographia Vertebral per Injection Retrograde in le Arteria Carotic Dextero-Commun

Arteriographia vertebral esseva executate per le percutanee injection retrograde del substantia de contrasto in le arteria carotic dextero-commun, durante que le distal arteria carotic commun e le arterias dextero-brachial esseva comprimite. Un arteriogramma vertebral de qualitate diagnostic esseva obtenite in 42 de 60 patientes (70 pro cento).

Injection retrograde in arteria carotic dextero-commun es utile in demonstrar le arterias dextero-subclavian e le portiones proximal del arterias carotic dextero- e sinistro-commun e del arterias dextero-vertebral. Le uso principal del methodo retrograde in le clinica del autores esseva in patientes con hemorrhagia subarachnoide.

Le insertion retrograde del agulia arterial in le arteria carotic commun evita le risco de un infilation del puncta del agulia in afficite segmentos de vaso in patientes con thrombose del interne arteria carotic in le collo.

False Block of the Internal Carotid Artery During Angiography[1]

WILLIAM E. GANNON, M. D.[2]

SINCE MONIZ *et al.* (1) in 1937 demonstrated occlusion of the internal carotid artery by angiography, the procedure has become increasingly the method of choice in the diagnosis of that condition. Palpation of the vessel in the neck or throat is not a reliable procedure because of the difficulty in separating the pulses of the internal and external carotid arteries (2–4). Historically the diagnosis of occlusion of the internal carotid artery has rested upon failure to opacify it in the presence of opacification of the common and external carotid arteries. Doubts concerning the reliability of this method have arisen, however, because of non-visualization of the artery during angiography in some cases in which subsequent operation or autopsy showed no obstruction. Riishede and Ethelberg (7) have reported 5 such cases, and Horwitz and Dunsmore (8) 4. The purpose of this paper is to present the roentgen findings in this condition and to suggest a possible etiology.

All examinations were performed with a serial cassette changer, with a minimum of six consecutive exposures in one projection and an interval of one second between exposures. Local procaine infiltration and occasional premedication with phenobarbital were employed. The needle was inserted percutaneously and 8 c.c. of 50 per cent Hypaque was injected manually. The first film was exposed just before the completion of the injection. Since all the procedures were performed in the same manner, the timing of the exposures in the various cases is roughly equivalent.

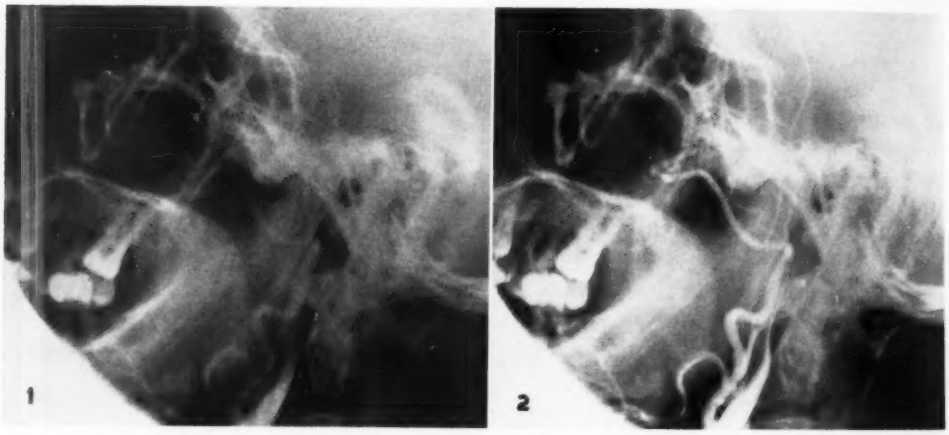


Fig. 1. Case I. One-second film, showing opacification of the internal carotid artery up to a point about 2 cm. below the base of the skull. The opaque column has a rounded upper border which is partially hidden by the external carotid artery.

Fig. 2. Case I. Six-second film. The contrast material in the internal carotid artery has become diluted. The opacification of the external and internal maxillary arteries is more intense, but there has been no progression of the contrast material through them.

CASE I: A 59-year-old Puerto Rican male was well until one year prior to admission, when he first experienced intermittent frontal and left temporal

[1] From the Departments of Radiology, State University of New York, Downstate Medical Center, Brooklyn, N. Y., and Kings County Hospital, Brooklyn, N. Y.– Accepted for publication in October 1960.

[2] Assistant Professor of Radiology.

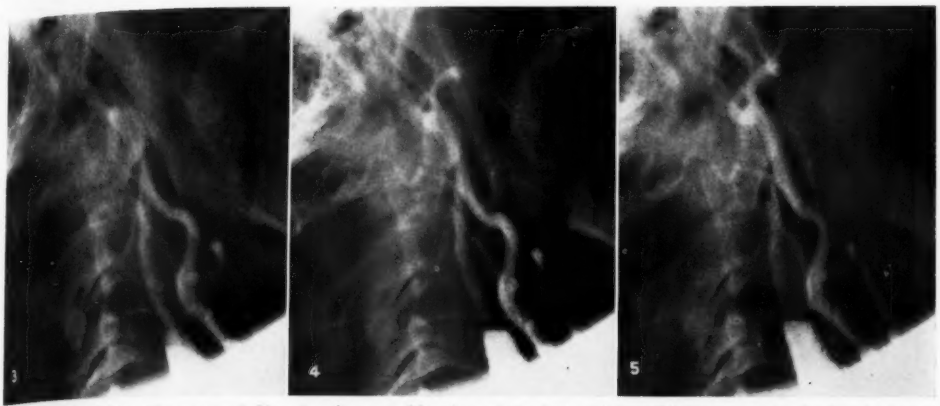


Fig. 3. Case II. Two-second film showing opacification of the internal carotid artery up to the level of C-1. A line of demarcation is starting to appear in the lower portion of the vessel.
Fig. 4. Case II. Three-second film showing the smooth upper border of the contrast material in the lower portion of the internal carotid and the radiolucent zone separating it from that in the upper portion.
Fig. 5. Case III. Six-second film. The radiolucent zone has become wider. There is no progression of the contrast material through the external carotid system.

headaches of moderate intensity. About seven months prior to the final admission, the pain increased in severity and became localized to the region of the left jaw, left ear and periauricular region, and the left eye. Because of the increasing severity of the pain, the patient was admitted to the hospital for study in July 1959. Physical and neurological examinations were completely negative at the time of this admission.

Left carotid angiography revealed opacification of the internal carotid artery up to a point about 2 cm. below the base of the skull on the initial film (Fig. 1). The external carotid and internal maxillary arteries were faintly opacified. The opaque column in the internal carotid artery had a rounded upper border which was partially hidden by the external carotid artery. The later films in the series revealed an increase in opacification of the external carotid vessels but no progression of the contrast material through them. At the same time there was dilution of the medium in the internal carotid (Fig. 2). The patient refused further work-up and signed his release.

He was seen in clinic a few months later, complaining of the same symptoms as before and was readmitted to the hospital on Nov. 20, 1959. Again the physical and neurological examinations were completely negative. On Dec. 1 the patient was seen to be in severe pain. There was obvious enlargement of the left parotid region, which was tender and firm. Administration of atropine promptly relieved the pain.

On Dec. 7 left carotid angiography was repeated. The contrast material progressed rapidly through the internal carotid artery and there was no evidence of narrowing or occlusion. A pneumoencephalogram obtained on Jan. 5, 1960, was normal. The spinal fluid at that time was clear and there was a negative Pandy test. The patient's pains continued to be controlled with atropine and he was eventually discharged with the diagnosis of Costen's (temperomandibular) syndrome.

CASE II: A 64-year-old white male, known to have had hypertension for many years, was admitted on Dec. 9, 1959, with a history of a cerebrovascular accident one year previously. There had been residual left-sided weakness which was gradually clearing. Following this episode the patient had been well until the day of admission, when he experienced several generalized seizures. On physical examination he appeared drowsy, restless, disoriented, and incoherent. He had a left homonymous hemianopsia, left central facial weakness, and hypalgesia of the left side of the face. The left extremities were weak, with moderate spasticity. The deep tendon reflexes were increased on the left side and there was a positive left Babinski toe sign. Lumbar puncture revealed a slightly increased initial pressure and a normal closing pressure. The fluid was clear and the Pandy test was negative. Within the next two days the patient became alert, coherent, and oriented. The homonymous hemianopsia, central facial weakness and hypalgesia, and Babinski toe sign disappeared. The weakness and spasticity of the left extremities were somewhat decreased. Retinal artery pressure readings obtained on the second day were 136/92 gm. in the right eye and 138/102 gm. in the left eye.

Right carotid angiography was performed on Dec. 17. Immediately after injection the patient went into shock and became semicomatose, with development of flaccidity of all extremities, bilateral Babinski toe signs, and deviation of the eyes to the left. The blood pressure dropped to 60/0 from a preinjection pressure of 200/125. Intravenous administra-

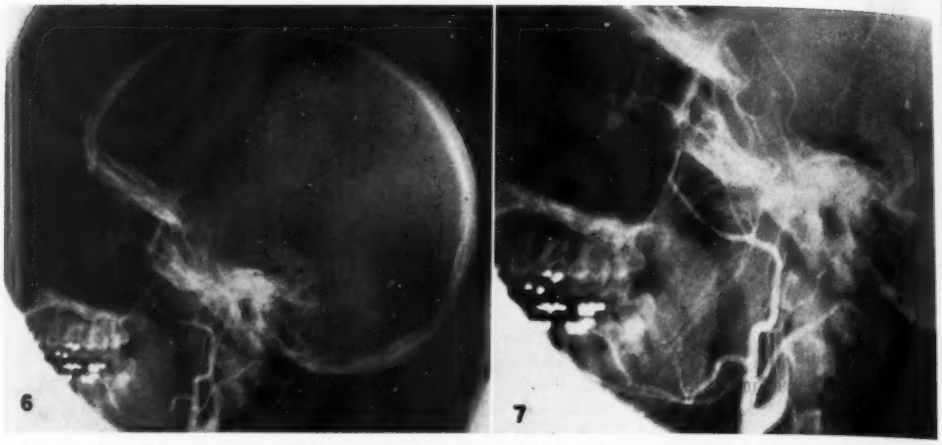


Fig. 6. Case III. Two-second film. The internal carotid is opacified up to the base of the skull.
Fig. 7. Case III. Four-second film. The contrast material in the internal carotid artery has been diluted. The opacification of the external system is intense, but there has been no progression of the opaque material through it.

tion of neo-Synephrine eventually restored the blood pressure to normotensive levels. This drug had to be continued for the next twenty-four hours, during which the patient remained drowsy and the neurological signs slowly disappeared.

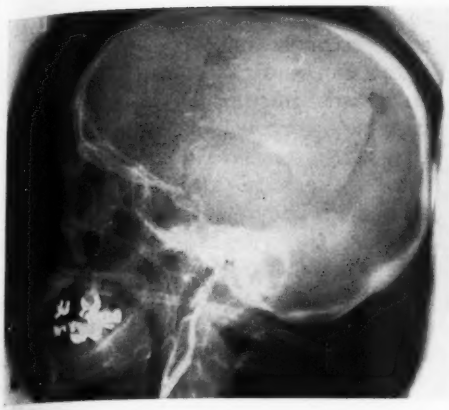
The second film of the series showed faint opacification of the internal carotid artery up to the level of the odontoid process (Fig. 3). On later films the vessel was faintly opacified up to the base of the skull but not beyond that point; the proximal portion became intensely opacified, with a smooth upper border (Fig. 4). This area of intense opacification gradually became separated by a radiolucent zone from the faintly opacified upper portion (Fig. 5). This separation presumably occurred when the patient went into shock. The external carotid artery and internal maxillary artery were intensely opacified, but there was no progression of the contrast material through this system.

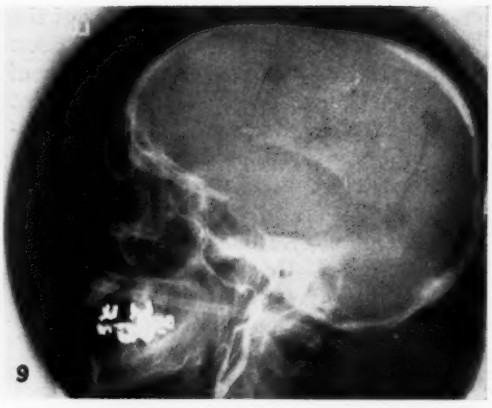
On Feb. 19, 1960, angiography was repeated. Multiple serial films of the neck failed to reveal any evidence of narrowing or obstruction of the internal carotid artery. The patient was discharged with the diagnosis of convulsive disorder due to a previous cerebrovascular accident.

CASE III: A 19-year-old Negro female was in good health until three years prior to admission, when she fell and struck her head. Following this accident, she experienced attacks of shaking of the right hand, arm, and shoulder. These were preceded by a feeling of impending attack but no visual or auditory aura were experienced. The patient would occasionally bite her tongue during these episodes but would never lose consciousness. She was brought to the hospital on Jan. 6, 1960, because of one of these attacks, during which she had become quite agitated and confused. Upon admission, physical examination disclosed a slight degree of dysarthria, a right central facial weakness, and slightly hyperactive right biceps and triceps reflexes. The patient gradually became alert but continued to have seizures while on the ward.

On Feb. 1, 1960, left carotid angiography was performed. On the second film after injection the internal carotid artery was opacified up to the base of the skull (Fig. 6). The external carotid, internal maxillary, and proximal portions of the superficial temporal and meningeal vessels were also visualized. In later films (Fig. 7) the contrast material in the cervical portion of the internal carotid artery was diluted, but at no time was the intracranial portion of this vessel visualized. The external vessels maintained their opacification, but there was little or no progression of the contrast material through them. Retinal artery pressures determined two days later showed 116/54 gm. in the right eye and 122/52 gm. in the left eye. The left carotid angiogram was repeated on Feb. 11 and there was no evidence of occlusion of the artery. The patient was discharged with the diagnosis of jacksonian epilepsy.

CASE IV: A 47-year-old white female underwent operation at another hospital for an astrocytoma, grade 2, of the temporal lobe. The tumor was too extensive for surgery and only a biopsy was performed. A full course of radiation therapy was then administered. Postoperatively the patient refused to eat and her course was progressively downhill. She was admitted to the Kings County Hospital (Brooklyn, N. Y.) on March 14, 1960, in a semicomatose state. There was a bulging left subtemporal bone flap, a right homonymous hemianopsia, right central facial paresis, spasticity of the right arm, severe paresis of the right leg, and a mild right hemihypalgesia.





Left carotid angiography was performed on March 18. On the initial film the internal carotid artery and a few branches of the middle cerebral artery were opacified (Fig. 8), as were also the external carotid and the internal maxillary artery. Following this the contrast material disappeared from the intracranial portion of the internal carotid. The cervical portion and the external and internal maxillary arteries remained well filled (Fig. 9). On the four-second film the intracranial portion of the internal carotid was again visualized, and the contrast material had now started to progress through the distal portions of the external carotid system (Fig. 10). At five seconds, the anterior and middle cerebral arteries were visualized. A repeat examination was immediately performed and the contrast material flowed without hesitation through the internal and external carotid systems.

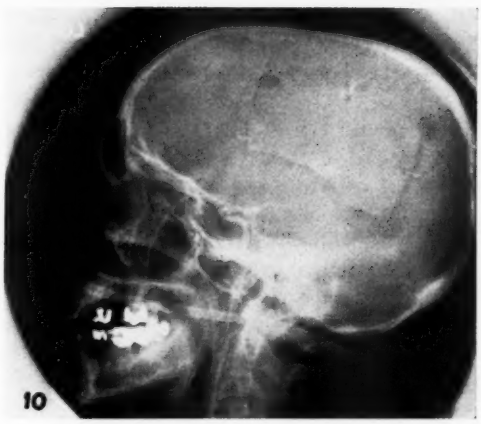


Fig. 8. Case IV. Initial film showing opacification of branches of the middle cerebral artery. On the original film the intracranial portion of the internal carotid artery can be faintly seen.

Fig. 9. Case IV. Three-second film. Contrast material has disappeared from the intracranial portion of the internal carotid. The external carotid and internal maxillary arteries are well opacified.

Fig. 10. Case IV. Four-second film. The intracranial portion of the internal carotid is opacified. Progression of the contrast material is evidenced by non-visualization of the neck vessels.

DISCUSSION

Johnson and Walker (5), reviewing 107 cases of thrombosis of the internal carotid artery, state that non-visualization of this vessel in the absence of occlusion occurs occasionally during angiography because of a technical error. Riishede and Ethelberg (7) and Horwitz and Dunsmore (8) believe that severe compression of the sympathetic and parasympathetic centers in the medulla as a result of increased intracranial pressure leads to a depressor reflex with resultant drop in cerebral blood flow. The absence of increased intracranial pressure in 3 of our cases would tend to rule this out as an explanation. Riishede and Ethelberg also suggest that a very generous external carotid circulation might tend to gain the majority of the contrast material. If this were so, we would expect non-visualization of the internal carotid artery to be found more frequently in the fairly large number of cases in which the needle is inserted into the proximal external rather than the internal or common carotid artery. This, however, is not the case. Tarnow (6) believes that the condition is due to reflex spasm following repeated needle punctures. It is hardly conceivable that a large blood vessel such as the internal carotid artery could become spastic so abruptly as to give

the smoothly rounded upper border of the opaque column that we see in these cases. If spasm were the cause, the vessels of the external carotid system should also become spastic. If anything, in this condition they appear dilated.

Foltz and co-workers (9) observed the effect of 35 and 70 per cent Diodrast on the pial vessels of monkeys and cats by means of a Forbes window and took simultaneous electroencephalographic and electrocardiographic recordings. They found that the contrast material caused severe vascular spasm of short duration followed by vascular dilatation for a much longer period. They concluded that there was a neuronal effect as well. This latter effect they postulated because of marked changes in the electroencephalogram which they grouped into negative and positive. The negative effect was characterized by reduction in amplitude of rhythmic discharges. It occurred during the terminal half of the Diodrast injection and usually lasted for ten to twenty seconds, although the duration was occasionally one to two minutes. The positive effect manifested itself by an increase in amplitude of rhythmic discharges and the production of new wave forms. It appeared much later. The electrocardiographic changes observed were loss of the P wave during the period of injection, bradycardia with intermittent loss of P waves, and ventricular extrasystoles. The same electroencephalographic and electrocardiographic changes were observed in man. Controls of isotonic saline caused no changes in either animals or man. Epstein *et al.* (10) obtained electrocardiograms of patients during carotid angiography. They found electrocardiographic changes in 72.5 per cent of 80 injections of Hypaque and Diodrast. These changes consisted of slowing of the heart rate from 19 to 40 beats per minute and, in the more severe cases, sinus arrest followed by ventricular escape with shift of the cardiac pacemaker to the coronary sinus or the atrioventricular node. Control isotonic saline injections were given to the same patients and none showed electrocardiographic changes.

Broman and Olsson (11) demonstrated an increase in permeability of the cerebral vessels to trypan blue following the injection of concentrated Diodrast solution into the carotid artery of experimental animals. They also noted a drop in blood pressure, the severity of which was directly proportional to the increase in permeability of the cerebral vessels. In the more severe cases, bradycardia was also noted. Many authors (12–16) have noted vasodilatation and fall in blood pressure following the injection of contrast material. Some (14, 16, 17) have suggested that these effects are due to a direct chemotoxic action of the contrast material on the endothelial membrane, causing paralysis of the smooth muscle of the arterial wall. The fact that concentration rather than amount of injected material (14, 16) is the determining factor in the production of these effects would tend to support this idea.

The carotid sinus, situated at the bifurcation of the common carotid artery or the origin of the internal carotid artery, is one of the most important structures in the control of cardiac rate and blood pressure. It is supplied with numerous free nerve endings in the adventitia of the vessel. These nerve endings are stretch receptors. Their afferent arc is through the glossopharyngeal nerve to the vasomotor center in the medulla, and the efferent arcs are the vagus nerve to the heart and the sympathetic innervation to blood vessels through lower centers in the spinal cord. Increase in blood pressure in the carotid system causes dilatation of the sinus with subsequent increase in the tonic discharges of these nerve endings to the vasomotor center. If the smooth muscle in the wall of the artery is paralyzed by the contrast material, the same result is obtained. With muscular relaxation the lumen will dilate and the stretch receptors will be activated. This will cause generalized vasodilatation and slowing of the heart because of increased vagal activity.

The final result will be a drop in blood pressure of varying degree. A severe response could result in shock such as occurred in Case II of our series. A mild response would cause a temporary halt in the progress of the opaque column, as in Case IV. This latter case would also correspond to what Ecker has termed "pseudo-spasm" (21).

Epstein and co-workers (10) infiltrated the carotid sinus area with procaine in 6 patients who had previously exhibited electrocardiographic reactions. After effective block of the carotid sinus in 5 patients, repeated arterial injections failed to elicit the previous vagal responses. In 1 patient who had an incomplete block only, the slightest cardiac slowing was elicited. This strongly suggests that routine infiltration of the carotid bifurcation should be performed to prevent the occurrence of false blocks of the internal carotid artery.

Riishede and Ethelberg and Horwitz and Dunsmore comment on the intense opacification of the common and external carotid arteries in their cases. This has been our experience also. However, the contrast material does not progress through this system, suggesting a generalized drop in blood pressure rather than a localized effect in the internal carotid artery. We feel that this failure of the opaque material to progress through the external carotid system is the most important diagnostic sign of a false block of the internal carotid artery.

Another significant finding is the appearance of the upper border of the contrast material in the internal carotid artery. If it has a rounded, meniscus, or completely flat appearance, the observer should immediately be alerted to the possibility of a false block. In such cases careful observation of the circulation through the external carotid system will usually confirm or rule out this diagnosis.

When a false block is suspected, angiography should be repeated after blocking of the carotid sinus by local procaine infiltration. Measurement of the retinal artery pressures is also a most useful procedure. Milletti (22) has pointed out the importance of determining retinal artery pressures in the presence of suspected thrombosis of the internal carotid artery. He stated that the systolic retinal artery pressure is decreased on the side of the lesion, although the diastolic retinal artery pressures may be equal.

Gurdjian and Webster (23–25) have advocated compression of the contralateral common carotid artery in cases of suspected occlusion of the internal carotid. If there is a definite occlusion, syncope or convulsions should occur within a short period of time. We have had no experience with this test but feel that it should be useful in suspected cases of false block of the internal carotid artery.

CONCLUSIONS

1. The absence of contrast material in the internal carotid artery is not sufficient evidence for making a diagnosis of occlusion of that vessel.

2. Failure of the internal carotid artery to opacify may be due to a drop in blood pressure mediated through a carotid sinus reflex.

3. If the upper border of the opaque column in the internal carotid artery has a rounded, meniscus, or flat appearance, the possibility of a false block should be suspected.

4. The passage of the contrast material through the external carotid artery and its branches should be noted to determine whether or not there is a slowed circulation in this system. Failure of the medium to progress through the external carotid system is the most important sign of a false block of the internal carotid artery.

5. Multiple serial films are of the utmost importance.

6. In questionable cases the examination should be repeated after the carotid sinus has been blocked.

7. Measurement of retinal artery pressures will help to rule out an occlusion of the internal carotid artery.

8. Digital compression of the opposite common carotid artery should be a useful procedure in suspected cases of false block.

450 Clarkson Ave.
Brooklyn 3, N. Y.

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SUMMARIO IN INTERLINGUA

Bloco False del Interne Arteria Carotic Durante le Angiographia

Ben que angiographia es le methodo de election pro le demonstration de occlusion del interne arteria carotic, casos occurre in que non-visualisation del vaso suggere un bloco ben que nulle tal es presente. Iste occurrentia de non-opacification pote esser le effecto de un declino del tension de sanguine que es mediate per un reflexo de sino carotic.

Le plus importante signo radiologic de bloco false del interne arteria carotic es le non-passage del medio opac per le systema carotic externe. Un altere signo de importantia es le arrondate, crescentiforme, o platte apparentia del margine superior del columna de opacitate intra le arteria.

Expositiones in serie es importante pro le diagnose, e in casos de dubita, le examine deberea esser repetite post blocage del sinus carotic.

Determinationes del tensiones arterial e compression digital del arteria carotic commun al altere latere es recommendate como utile adjutas diagnostic.

Effects of Intensive Radiation on the Human Heart[1]

JEROME M. VAETH, M.D., LAWRENCE Z. FEIGENBAUM, M. D., and MALCOLM D. MERRILL, M. D.

RECENT AWARENESS of the effect of radiation on the heart reflects the revived interest in the radiobiologic reaction of normal tissue. As early as the first two decades following the discoveries of Roentgen and the Curies, the radiation effect on normal tissue was under study. The astuteness and prophetic vision of the early investigators are well reflected in such reports as Lacassagne and Gricouroff's *Action des radiations sur les tissus*. Later, as knowledge of the biologic effect of radiation increased, emphasis in the literature shifted to the therapeutic effects of ionizing radiation on neoplasms. Now, with improved apparatus and technics permitting larger doses of radiation not dependent solely on skin tolerance, the previously accepted dogma on normal tissue reaction requires reappraisal.

An excellent general review of the radiologic literature on the effect of radiation on the heart has recently been made by Jones and Wedgwood (2). As early as 1897, Sabrazès and Rivière (4) reported the effects of roentgen rays on the frog's heart. In the same year, Seguy and Quénisset (5) published their observations of a patient whose precordial region was exposed to roentgen rays.

Gloriozov (1), in 1949, reported the clinical and electrocardiographic effects of radiation on the heart in 10 patients treated for esophageal or lung neoplasm. He concluded that large doses of radiation produced sinus tachycardia, extrasystoles, and degenerative changes in the myocardium. Until that time, the heart had been considered relatively immune to doses of radiation administered in amounts consistent with the technic of those earlier years.

In 1957, Whitfield and Kunkler (6) described 4 patients in whom electrocardiographic changes developed during or following radiotherapy to the thorax including the cardiac area.

A series of 25 female patients who had received roentgen treatment for carcinoma of the breast was studied by Jones and Wedgwood for nonspecific electrocardiographic changes. This was the first carefully observed series consisting of a relatively large number of patients. The investigators pointed out that most of the cardiac disturbances previously reported as resulting from irradiation fit into two groups: (*a*) arrhythmias and (*b*) "extracardiac mediastinal disturbances." They found no evidence that arrhythmias are attributable to radiation; mediastinopericardial reactions, which they consider the more important, are rare. Jones and Wedgwood also noted nonspecific ST-T wave changes several weeks following roentgen therapy. Although the nonspecific changes observed may have been due to mediastinal disturbances, other factors such as electrolyte disturbances, positional changes, and myocardial damage remain as possible causes.

In treating intrathoracic neoplasms and postoperative breast carcinomas, particularly with supervoltage roentgen rays, large doses of radiation are delivered to the heart. This report concerns the observations on 20 such patients, most of whom received doses in the cardiac area of more than 3,500 r.

METHOD

Twenty consecutive patients, 11 males and 9 females, whose ages ranged from twenty-three to seventy-three years (average 44.9 years) were selected for this study. All had malignant tumors necessitating radiation therapy involving at least 35 per cent of the myocardium. The

[1] From the University of California, School of Medicine, San Francisco, Calif. (J.M.V. and M.D.M., Department of Radiology; L.Z.F., Department of Medicine.) Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4–9, 1960.

TABLE I: CORRELATION OF CARDIAC DOSE AND ABNORMAL FINDINGS

Case No.	Age Sex	Diagnosis	X-Ray (Mev)	Fields Thoracic (cm.)	Cardiac Dose (Days)	Cardiac Symptoms and Signs	ECG Changes	SGOT Changes	Status	Autopsy
1	25 M	Testicular ca., mediastinal metas.	1	AP PA 12 × 13	1000 r 14	No	No	Yes	Dead	No
2	65 F	Breast ca., postop.	1	AP 7 × 15	2400 r 23	No	Yes	No	Dead	No
3	44 F	Renal ca., pulm. metas.	1	AP 10 × 10	2700 r 20	No	No	No	Dead	No
4	54 F	Breast ca., postop.	1	AP 7 × 15	2900 r 30	No	No	No	Alive Sept. '60	...
5	51 M	Esophageal ca.	1	AP PA 8 × 17	3000 r 26	No	No	No	Dead	No
6	50 M	R.E. sarcoma, thoracic spine, mediastinum	1	AP PA 9 × 12	3500 r 45	No	Yes	Yes	Dead	No
7	27 F	Hodgkin's dis., mediastinum	1	AP PA 13 × 13	3600 r 48	No	No	No	Alive Sept. '60	...
8	52 F	Breast ca., postop.	1	AP 7 × 15	3600 r 34	No	No	No	Alive Sept. '60	...
9	33 F	Breast ca., postop.	1	AP 5 × 14	2900 r 39	No	No	Yes	Alive Sept. '60	...
10	48 M	Lung ca., oat-cell	1	AP PA 11 × 15	4000 r 23	No	Yes	No	Dead	No
11	31 F	Hodgkin's dis., mediastinum	1	AP PA 12 × 17	4000 r 49	No	No	No	Alive Sept. '60	...
12	32 F	Breast ca., postop	1	AP 7 × 15	4100 r 41	No	No	Yes	Alive Sept. '60	...
13	48 M	Lymphosarcoma, stomach, mediastinum	1	AP PA 8 × 12	4200 r 94	No	Yes	Yes	Alive Sept. '60	...
14	25 M	Hodgkin's dis., mediastinum	1	AP PA 7 × 17	4400 r 37	Yes	Yes	No	Alive Sept. '60	...
15	29 F	Breast ca., postop.	1	AP 6 × 15	4600 r 46	No	No	No	Alive Sept. '60	...
16	73 M	Esophageal ca.	1	AP PA 6 × 14	4700 r 58	No	No	No	Dead	No
17	55 M	Granulomatous thymoma, mediastinum	1	AP 14 × 14	5000 r 86	No	No	Yes	Alive Sept. '60	...
18	49 M	Bronchogenic ca.	1	AP 10 × 13	5700 r 63	No	Yes	Yes	Alive Sept. '60	...
19	56 M	Bronchogenic ca.	70	AP PA 8.5 × 10	6100 rads 40	No	Yes	Yes	Dead	Yes
20	58 M	Esophageal ca.	1	AP PA 7 × 15	6500 r 70	No	No	No	Dead	No

histologic types of neoplasm are shown in Table I. Each patient was thoroughly examined by the cardiologist (L.Z.F.). Electrocardiograms (ECG), serum glutamic oxalacetic transaminase (SGOT) determinations, sedimentation rates, and circulation times were obtained in every case prior to, during, and on completion of treatment. Because elevation of serum transaminase is known to accompany myocardial damage, this study was included. Elevated serum transaminase levels, however, may also occur when large volumes of tissue are irradiated and must be evaluated in the light of laboratory and electrocardiographic findings. In 10 of the 11 patients surviving six months, these examinations were repeated. A postmortem study was made in 1 of the 9 patients who died. Detailed examination of the heart, both gross and microscopic, was performed for evidence of cardiac damage incriminating irradiation.

Nineteen of the 20 patients received 1-Mev radiation. One patient was treated on the 70-Mev synchrotron. Field sizes ranged from 6 × 14 cm. for opposing anterior and posterior fields, to 14 × 14 cm. for a single anterior field. Localization films were taken on the treatment machine. The daily increment varied from 50 to 450 r (skin). The total dose and treatment time depended on the disease and response to treatment. In general, our patients satisfactorily tolerated a dose estimated at 750 r per week at the tumor level. The central cardiac dose was estimated by utilizing lateral chest roentgenograms without correction for passage of the beam through pulmonary tissues. The doses delivered to the heart were less than 3,000 r in 4 patients, between 3,000 and 5,000 r in 13 patients, and more than 5,000 r in 3 patients.

RESULTS

Of the 20 patients, 13 showed no electrocardiographic changes following radiotherapy. In 6 of these serum glutamic oxalacetic transaminase was not elevated; in 7 it was variable. Electrocardiographic changes were observed in 7 patients, associated with variable elevation of serum glutamic oxalacetic transaminase in 6, of whom 2 had pericarditis and 4 nondiagnostic T-wave changes. In the seventh patient, with no change in serum glutamic oxalacetic transaminase, the changes in the electrocardiogram were minor.

Nonspecific T-wave changes have been previously reported (2). T-wave inversions of V_1 to V_2, or V_1 to V_3, such as are reported by Whitfield and Kunkler, are most likely positional in origin and cannot be considered as positive evidence of myocardial damage.

Descriptions of the 6 patients with electrocardiographic changes follow.

Patients with Changes Interpreted as the Result of Pericarditis

CASE 14: A 25-year-old male was the only patient of the 20 with clinical evidence (substernal pain) of cardiac changes correlated with electrocardiographic findings. He was receiving roentgen therapy for a mediastinal mass diagnosed histologically as Hodgkin's disease. An electrocardiogram on the thirteenth day of treatment was normal (Fig. 1). Eighteen days after initiation of therapy at a dose estimated at 2,300 r to the heart, substernal chest pain occurred. A chest film at this time revealed a satisfactory regression of the mediastinal mass. Ten days later (twenty-eight days after the beginning of roentgen therapy) an electrocardiogram revealed ST elevations in V_2 to V_4, not previously present (Fig. 2). These changes were interpreted as probably indicating pericarditis. Serum glutamic oxalacetic transaminase determinations remained normal. At the completion of radiation therapy, at which time 4,400 r had been delivered to the heart (nineteen days after the onset of chest pain), both the pain and electrocardiographic evidence of pericarditis had disappeared (Fig. 3). An electrocardiogram eight months after radiation therapy was normal.

The symptoms and electrocardiographic evidence of pericarditis in this case were thought to have been induced by radiation rather than by involvement of the pericardium by progressing neoplasm, since roentgenograms obtained at the same time showed minor regression of the mass.

CASE 13: A 48-year-old male was under treatment for a lymphosarcoma involving the stomach as well as the celiac and mediastinal lymph nodes. Surgical and pathologic evidence of pericardial involvement by extension from the mediastinal nodes was present. Electrocardiograms prior to and during the initial week of radiation therapy were normal

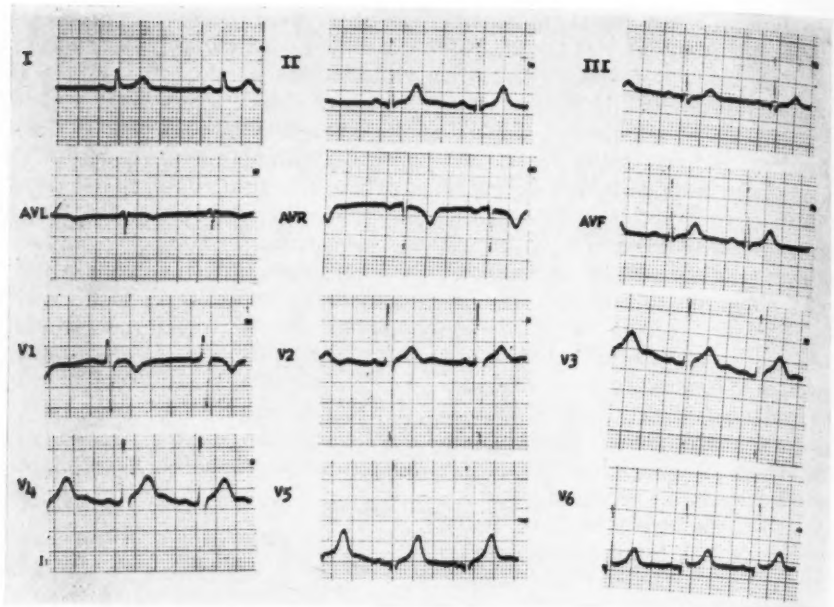

Fig. 1. Case 14. Normal appearing electrocardiogram on thirteenth day of roentgen treatment.

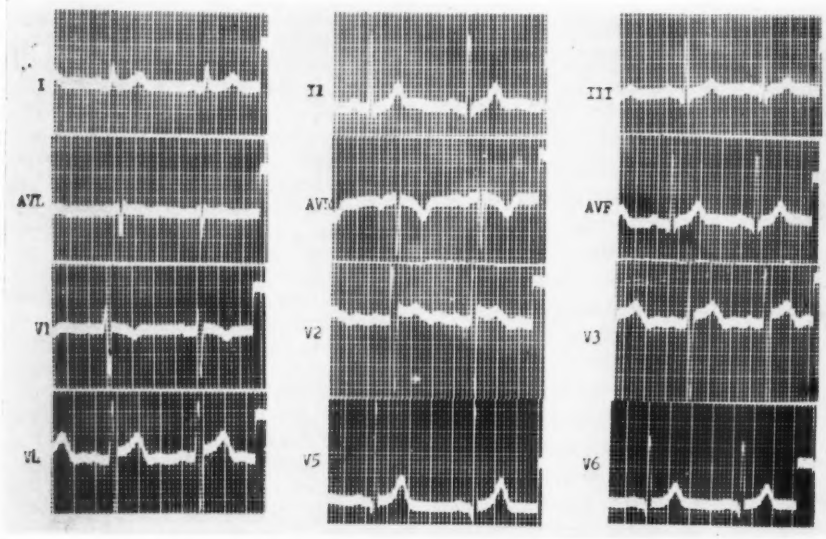

Fig. 2. Case 14. Electrocardiogram twenty-eight days after institution of roentgen therapy. ST elevations in V_2 to V_4 interpreted as probably indicative of localized pericarditis.

(Fig. 4), despite the known lymphosarcomatous involvement of the pericardium. Definite ST elevations, consistent with pericarditis, were seen on the fourteenth day of treatment, at which time an estimated dose of less than 800 r had been delivered to the heart (Fig. 5). No related symptoms were reported by the patient. Twelve days later the electrocardiogram showed no evidence of pericarditis. The patient received a cardiac dose of 4,200 r in nine weeks. Nine months following roentgen therapy, the electrocardiogram was normal (Fig. 6).

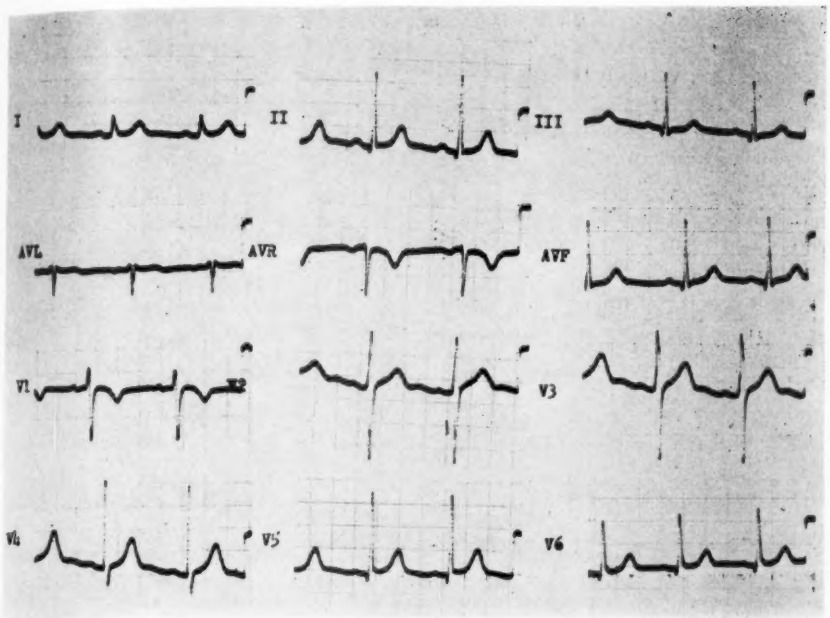

Fig. 3. Case 14. Electrocardiogram at completion of therapy. Evidence of pericarditis has disappeared.

Patients with Abnormal Electrocardiograms and Elevated Serum Glutamic Oxalacetic Transaminase Determinations

CASE 6: A 50-year-old male was treated for a reticuloendothelial sarcoma involving several segments of the thoracic spinal cord and extending by direct continuity into the mediastinum. The electrocardiogram and serum glutamic oxalacetic transaminase determinations were normal prior to initiation of roentgen treatment. On the eighth day of therapy, when only 500 r had been delivered to the cardiac area, the serum glutamic oxalacetic transaminase was elevated to 43 units (pretreatment, 25 units). At that time slight T-wave depressions were noted in Leads II and III and in V_1, which were still present eight days afterward. These findings reverted to normal approximately four weeks later. An estimated total dose of 3,500 r to the heart was delivered in forty-five days. In this patient, although the association between electrocardiographic changes and serum glutamic oxalacetic transaminase elevation suggests the possibility of myocardial damage, it is unlikely that a dose of 500 r in eight days could have caused these changes.

CASE 19: A 56-year-old male was treated on the 70-Mev synchrotron for a bronchogenic carcinoma of the right main-stem bronchus. Prior to the initiation of therapy, a right bundle-branch block was noted on the electrocardiogram. The serum glutamic oxalacetic transaminase determination was normal. Seven days after the initiation of radiation therapy at a cumulative dose of 1,000 rads to the cardiac region, a sinus tachycardia and slightly increased T-wave inversions were noted. By the thirty-fifth day of therapy the electrocardiogram had reverted to its pretreatment pattern. The serum glutamic oxalacetic transaminase values remained normal at the time of the electrocardiographic changes but rose at the termination of radiation therapy.

The findings in this case are not conclusive of myocardial damage. The slight T-wave changes could well have been the result of a nonspecific cause. A total dose of 6,100 rads in forty-one days was delivered to the heart. Death occurred seven months after completion of radiation therapy. At autopsy, gross and microscopic studies of the heart showed no abnormalities related to radiation, despite the large dose administered.

CASE 10: A 48-year-old male was treated for lung carcinoma of the oat-cell type. An electrocardiogram taken after exploratory thoracotomy and prior to initiation of roentgen therapy revealed nonspecific T-wave flattening. At this time serum glutamic oxalacetic transaminase elevation was observed. Fourteen days after irradiation was begun, and again at its completion, both the electrocardiogram and the serum transaminase level were normal. The patient received an estimated dose of 4,000 r

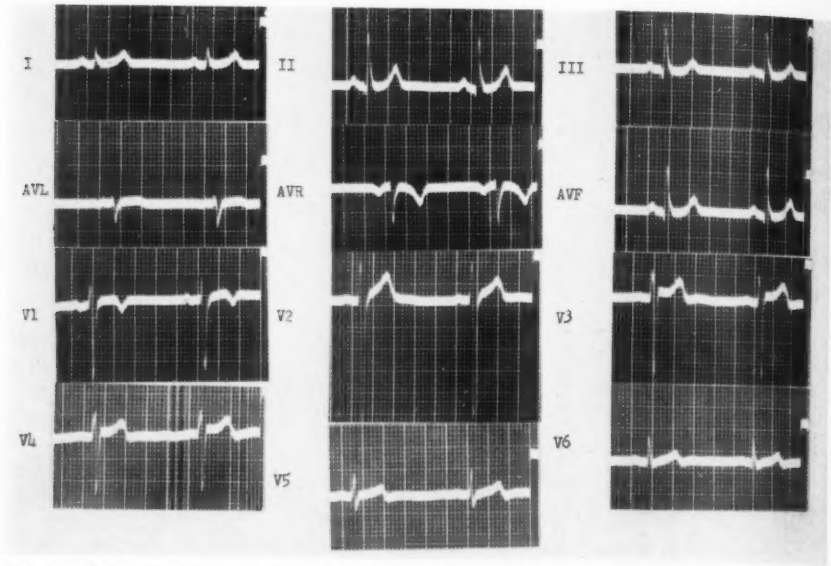

Fig. 4. Case 13. Normal appearing electrocardiogram prior to treatment, despite known pericardial involvement by lymphosarcoma.

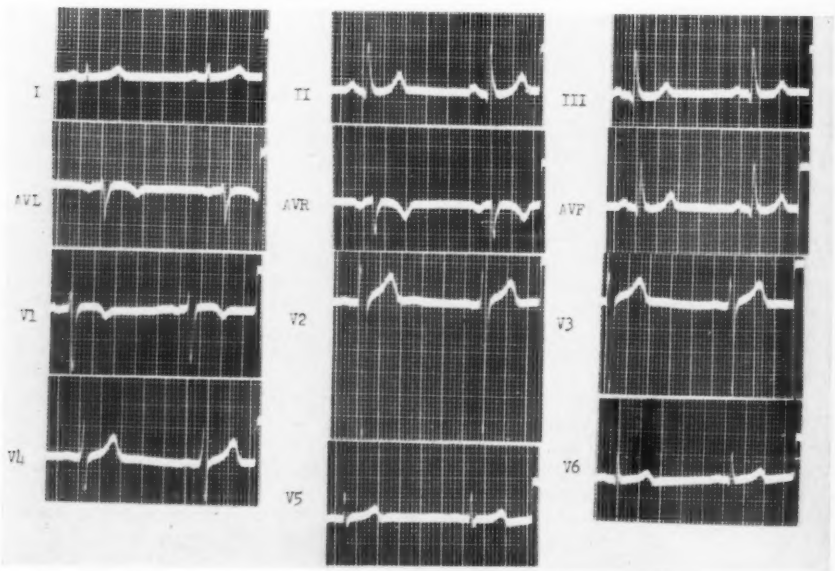

Fig. 5. Case 13. ST elevations in V_2 to V_4 consistent with localized pericarditis. These changes appeared on the fourteenth day of treatment, when an estimated dose of less than 800 r had been delivered to the heart.

to the heart in twenty-three days. Four weeks after completion of radiation therapy a rise in the serum glutamic oxalacetic transaminase to 43 units was noted and nonspecific T-wave flattening was again demonstrated. These changes were not considered diagnostic of myocardial damage.

CASE 18: A 49-year-old male was treated for bronchogenic carcinoma. An electrocardiogram prior to therapy suggested left ventricular hypertrophy. The serum glutamic oxalacetic transaminase was normal (25 units). On the eighteenth day of therapy, at which time the patient had received ap-

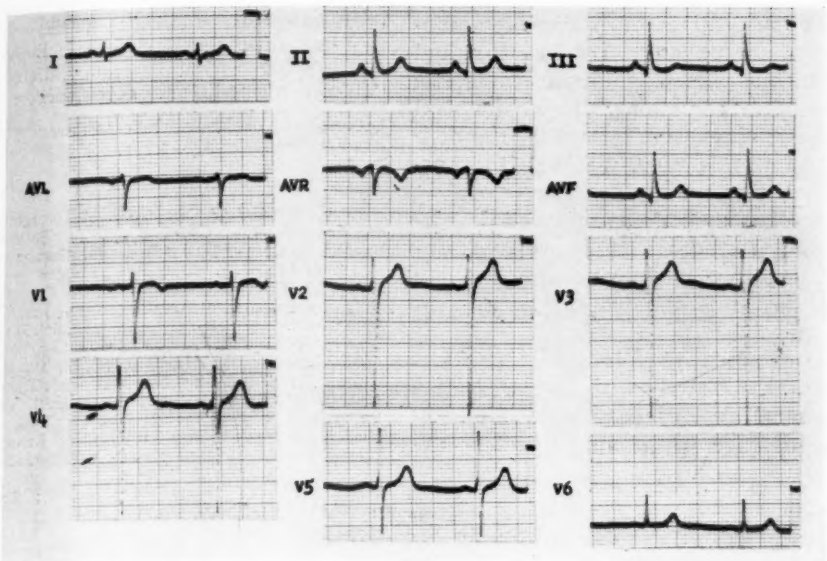

Fig. 6. Case 13. Normal appearing electrocardiogram obtained nine months after roentgen therapy.

proximately 1,800 r to the heart, slight T-wave changes were noted; the serum glutamic oxalacetic transaminase was still not elevated. On the thirtieth day of treatment, with 3,000 r delivered to the heart, slight ST depressions were noted, also without serum transaminase changes. At the completion of therapy, at which time the heart had received 5,700 r, no abnormal electrocardiographic findings were noted, although the serum glutamic oxalacetic transaminase had become elevated to 72 units. This elevation was not associated with the nonspecific electrocardiographic findings.

Gross and Histologic Evidence of Cardiac Damage

One patient (Case 19) of the 9 succumbing to disease came to autopsy. Even though he had received an estimated dose of 6,100 rads to the heart in forty-one days, no evidence of cardiac damage was observed. It is interesting to note that a portion of the heart was in the radiation field, while the remainder was not. No difference could be detected, either grossly or microscopically, by the pathologist, on detailed examination of both irradiated and unirradiated cardiac tissue.

DISCUSSION AND SUMMARY

In 20 patients receiving large doses of radiation to the heart, no significant cardiac damage was detectable clinically or by electrocardiograms or serum glutamic oxalacetic transaminase determinations. In 1 patient who received over 6,000 rads to the heart, a detailed histologic examination showed no cardiac damage attributable to radiation.

In 2 patients electrocardiographic evidence of pericarditis developed during treatment for masses involving the mediastinum. The pericarditis was transient, did not interfere with continuance of radiotherapy, and had subsided completely at the end of treatment. Pericardial involvement was proved by surgery in 1 patient prior to the initiation of radiation therapy. In the other, at the time of development of the pericarditis, roentgenograms revealed the mediastinal mass to be diminishing in size. It is more likely, therefore, that the pericarditis was due to irradiation, rather than to the neoplastic disease. The absence of abnormal serum glutamic oxalacetic transaminase determinations is compatible with pericardial rather than with myocardial reaction.

In 4 patients with electrocardiographic

changes suggestive of reversible myocardial damage, only 1 (Case 6) had simultaneous serum glutamic oxalacetic transaminase elevations. It is doubtful that the findings were caused by the dose delivered at this time, although the possibility exists.

If cardiac damage is induced by irradiation, it appears to be of such insignificance that modification of adequate present-day radiotherapeutic technics is not justified.

It is planned to follow all survivors reported in this study with annual electrocardiograms in order to ascertain any cardiac damage which might become evident at a later time.

ACKNOWLEDGMENT: The authors are grateful to the American Cancer Society for funds permitting laboratory and electrocardiographic data on these patients. We also express thanks to Dr. Robert S. Stone for permission to include in this study a patient treated in the U. S. Atomic Energy Commission's Radiological Laboratory, University of California Medical Center, San Francisco, Calif.

University of California Medical Center
San Francisco 22, Calif.

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SUMMARIO IN INTERLINGUA

Effectos in le Corde Human, ab Radiation Intense

In 20 patientes recipiente large doses de radiation al corde, nulle significative damno cardiac esseva detegibile clinicamente o electrocardiographicamente o a base de determinationes del nivellos seral de transaminase glutamic-oxaloacetic. In le caso de un patiente, qui recipeva plus que 6.000 rad al corde, nulle damno attribuibile al radiation esseva evidente histologicamente.

In 2 patientes, indicationes electrocardiographic de pericarditis se disveloppava durante un therapia pro massas que afficeva le mediastino. Le pericarditis esseva transiente. Illo non interfereva in le continuation del radiotherapia e esseva completemente resolvite al tempore del completion del therapia. Un affection pericardial esseva demonstrate chirurgicamente in un de iste casos ante le institution del therapia a radiation. In le altere—al tempore del disveloppamento del pericarditis—roentgenogrammas revelava que le massa mediastinal vadeva diminuente in largor, e il pare per consequente in iste caso que le pericarditis esseva de facto le resultato del irradiation. Le absentia de anormalitate del valores seral pro transaminase glutamic-oxaloacetic es compatibile con le stipulation de un reaction pericardial plus tosto que myocardial.

In 4 patientes con alterationes electrocardiographic del typo associate con reversibile lesiones myocardial, solmente un monstrava un simultanee elevation del nivellos seral de transaminase glutamic-oxaloacetic. Il es dubitose que le radiation delivrate a ille tempore esseva responsabile. Nonobstante, le possibilitate existe.

Si damno cardiac es inducite del toto per irradiation, illo pare esser si minime que un modification del technicas radiotherapeutic currentemente reguardate como adequate non es justificate.

Es planate observar currentemente omne le superviventes del hic reportate serie per medio de annual examines electrocardiographic pro deteger omne damno cardiac que va possibilemente facer se evidente in le curso del tempore.

Percutaneous Cricothyroid Membrane Bronchography[1]

SAMUEL D. HEMLEY, M.D., EDWARD J. ARIDA, M.D.,[2] A. MONROE DIGGS, M.D.,[3] and SUMNER L. FREEMAN, M.D.[4]

OUR EXPERIENCE in the past six months with 42 consecutive transcricoid needle punctures has led us to conclude that this method of bronchography is safe, time-saving, practical, and effective. We have used this procedure to the complete exclusion of the more conventional transglottic catheterization technic.

In the past we had found the transglottic catheter method burdensome to the examiner and often intolerable to the patient. It was sometimes inadequate and frequently impossible of performance, especially in the large group of non-English speaking patients seen in our hospital. We sought, therefore, to change our technic to one more suitable not only to this type of patient, but also to the active schedule of our department.

The transcricoid needle method has been widely employed in England and Continental Europe. The first indication of renewed interest in this method appearing in the recent American medical literature was a paper by Beck and Hobbs (1). Our experience with the exclusive use of the transcricoid approach in the 42 consecutive bronchographic examinations has led to the development of the following method.

METHOD

Preparation of Patient: All patients studied were hospitalized and observed for twenty-four hours following the procedure.

The previous meal is withheld as a precaution against aspiration. Thirty minutes prior to the examination, appropriate doses of either atropine or scopolamine, and Demerol are given. Caution is observed against oversedation, since the patient is required to move about for distribution of the contrast medium and filming. The patient is placed supine on the fluoroscopy table, with a pillow or sandbag under the shoulders and the top of the head resting on the tabletop. This affords optimal hyperextension, which is indispensable.

The Needle Puncture: The cricothyroid membrane is a thin, avascular structure that stretches across the space between the anterior prominence of the thyroid cartilage and the anterior part of the cricoid cartilage. Palpation of the depression between these two structures in the anterior midline easily localizes this area. After preparation of the neck, with aseptic technic, the skin and subcutaneous tissue overlying the cricothyroid membrane are infiltrated with 1 per cent procaine hydrochloride. A 16-gauge beveled needle, 1 1/2 inches in length, is attached to a 2-c.c. syringe containing 1 c.c. of 2 per cent Pontocaine Hydrochloride. The syringe is tested to insure a freely movable plunger. With the base of the syringe held between the thumb and second finger, the needle is placed perpendicular to the skin overlying the cricothyroid membrane. The thyroid cartilage is stabilized with the thumb and second finger of the other hand. With firm and constant pressure, a sudden relaxation of resistance is felt when the membrane has been punctured and the subglottic tracheal space entered. The sensation is not unlike that experienced upon entering the dura in performing a lumbar puncture. Skill and confidence can easily be developed by performing the procedure initially on a cadaver. Figure

[1] From the Department of Radiology, St. Luke's Hospital, New York, N. Y. Samuel D. Hemley, M.D., Acting Director. Accepted for publication in October 1960.

[2] First Assistant Resident, Department of Radiology, St. Luke's Hospital, and National Institutes of Health Cancer Trainee.

[3] Resident, Department of Radiology, St. Luke's Hospital.

[4] Assistant Attending Otolaryngologist, St. Luke's Hospital.

1 shows the relation of the needle tip to the subglottic structures.

The plunger of the syringe is withdrawn and air enters the barrel if the needle lies in the tracheal canal. The patient is then tilted into a 10° Trendelenburg position and the 2 c.c. of the anesthetic solution is injected. (Proper positioning for the injection of the anesthetic is of great importance as will be shown.) The patient is assured that the tendency to cough and gag is short-lived. Panting is often helpful.

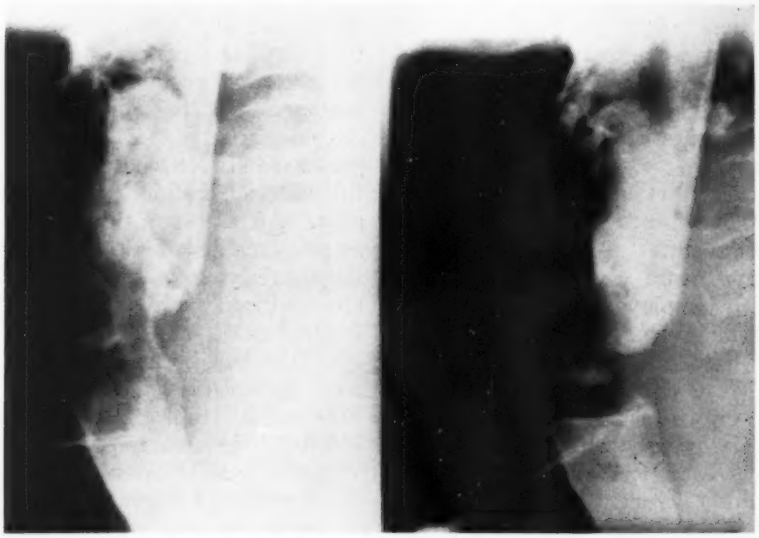

Fig. 1. Laryngogram indicating the position of the needle in relation to the glottic structures, obtained as a part of the bronchogram.

The syringe and needle are separated, and injection of the opaque material can be begun with the patient in any of the appropriate positions. Fixation of the needle is usually unnecessary if the patient can maintain adequate hyperextension of the head; however, the needle may be taped if desired. In the absence of free movement of the head or vigorous coughing, the needle will remain in place. Aspiration of air as a test of the position of the needle is recommended whenever the patient is moved into a new position or when additional medium is to be injected.

In filling the upper lobes there is no contraindication to tilting the patient into the deep Trendelenburg position. The gag reflex initiated by pharyngeal stimulation has been inhibited by instillation of the local anesthetic. This overcomes the objection by some authors, in the older literature, that gagging resulted when the contrast substance flowed into the supraglottic pharynx in an attempt to fill the upper lobes. We have never encountered this problem when anesthesia was induced in the manner described above. Several of the bronchograms have revealed opacification of the esophagus; and yet the patients at no time experienced any discomfort.

RESULTS

In 3 of the 42 transcricoid studies performed, complications occurred. Two of these were minor and were directly related to the procedure. In one patient subcutaneous emphysema developed but cleared without incident in three days. A second patient experienced hoarseness which lasted one day. In a third patient, immediately following an uncomplicated, atraumatic transcricoid study, a brisk

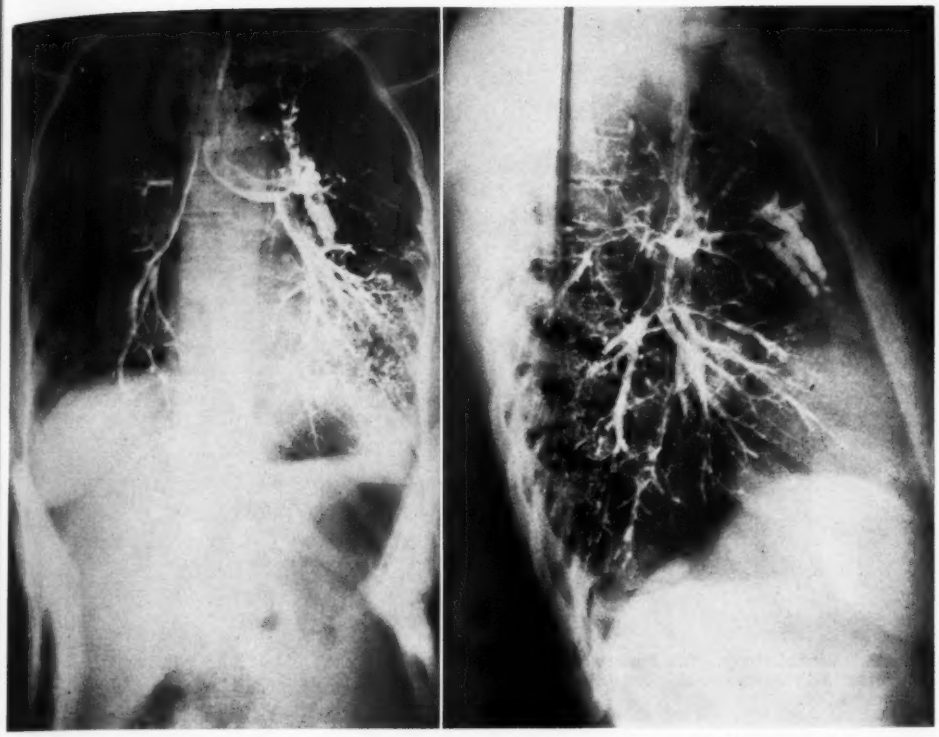

Fig. 2. Severe saccular bronchiectasis in anterior segment of left upper lobe, well demonstrated by percutaneous transcricoid bronchography; anteroposterior and lateral views. Proved at autopsy to be of tuberculous origin.

hemoptysis developed and death from cardiac arrest ensued during administration of anesthesia for bronchoscopy on the same day. Postmortem examination revealed a single small puncture in the cricothyroid membrane with minimal ecchymotic changes in the overlying soft tissue. The hemorrhage had presumably arisen from severe tuberculous bronchiectatic cavities in the left upper lobe and was not related to the needle puncture (Fig. 2).

All the patients tolerated the procedure well. Two who previously had been examined with the catheter voluntarily admitted a preference for the puncture method.

The examinations were completed swiftly, including fluoroscopy and tomography when indicated. The fluoroscopist can easily perform the needle puncture while dark-adapting. The effectiveness of this method in providing detailed anatomic studies of the bronchial tree in normal and pathologic states is demonstrated in Figures 3 to 6.

DISCUSSION

Transcricoid bronchography was initially described by Sicard and Forestier in 1922 (2). Although this method has remained in use in England and on the Continent, it has never been widely used or publicized in the United States. Several objections were raised against it in the past. Diehl (3) has summarized these as follows: (*a*) danger of inserting the needle into a nerve, blood vessel, or other vital structure; (*b*) the possibility of resulting subcutaneous or mediastinal emphysema; (*c*) possible complicating infection. Others have mentioned the inadvertent injection of the medium into paratracheal soft tissue.

Despite the possibility of these hazards,

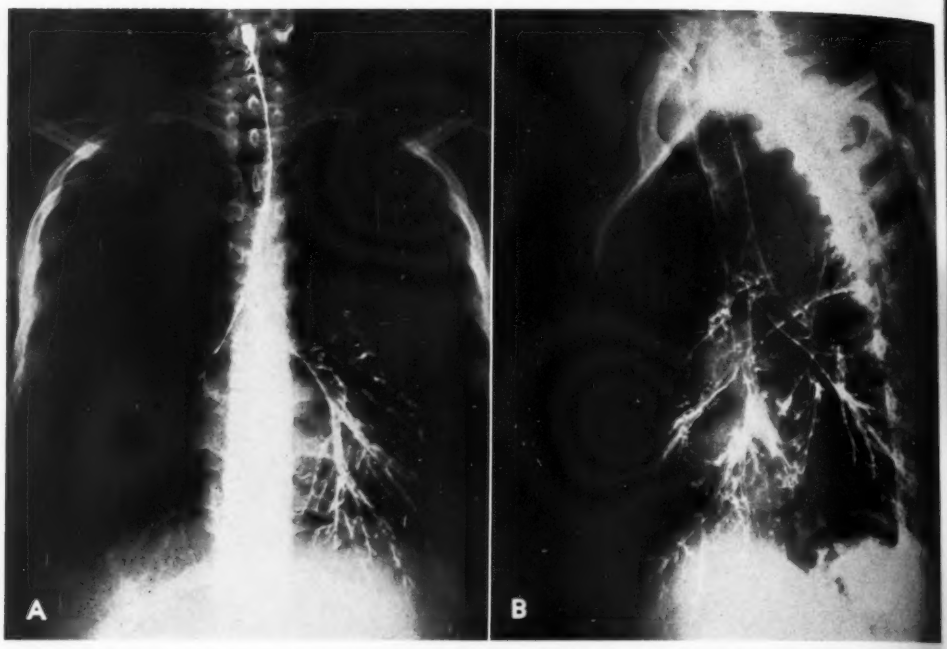

Fig. 3. Normal study. A. Postero-anterior projection with bronchi of left lung well demonstrated, indicating the ease with which one side can be studied alone with proper positioning. B. Left anterior oblique view, both sides filled.

they are extremely rare. Actual reports of significant complications have been distinctly isolated. For example, in a review of the literature, Willson (4) mentioned finding only 4 reports of serious complications. These included one of each of the following: transitory air embolus, a case of extravasation of the contrast material and abscess formation, fatal mediastinal emphysema, and a fatal anaerobic cellulitis.

A review of the recent American literature yielded only three articles dealing with transcricoid bronchography. Beck and Hobbs (1) in 1958 dealt specifically with the technic and indicated that they had used the procedure extensively with good results. They did not cite specific cases or complications. Willson (4) in 1959 recorded 25 cases, with no complications. He expressed a preference for this method, which resulted in better diagnostic films and less discomfort to his patients. Four out of five of these, who had previously been studied with the transglottic catheter, preferred the needle method. Willson suggested replacing the needle by a polyethylene catheter to eliminate the possibility of dislodging the needle and allowing more freedom of motion for the patient. This additional step in the procedure is optional and we have found it unnecessary. Finally, Reams and Bosniak (5) in 1959 reported 19 cases of transcricoid bronchography. They recorded two complications: a local cellulitis that responded to antibiotics and an instance of extravasation that cleared in twenty-four hours. These authors noted a much higher incidence of immediate reactions (syncope, bradycardia, etc.) related to the more conventional transglottic procedure. Five patients in this series were examined by both methods and all indicated a preference for the needle puncture.

Only 4 of the 86 transcricoid punctures now recorded in the recent American literature resulted in minor complications, all without sequelae. Extravasation of the presently available absorbable media ap-

pears to be of little consequence. Moreover, if care is taken to check the position of the needle by the frequent aspiration of air, extravasation should not occur. Subcutaneous emphysema was noted in only 1 of the recorded 86 cases and in this instance the patient insisted on moving his

Fig. 4. Chronic bronchitis. Right anterior oblique projection, both sides filled. Bronchiolectasis and adenolectasis demonstrated in a patient with chronic bronchitis and emphysema. Note contrast material in the esophagus.

head freely and swallowing frequently. Infection in this era of antibiotics becomes less significant than in the earlier days of this procedure, particularly if one adheres carefully to aseptic technic. Puncture of vital structures such as vessels and nerves seems to us an extremely remote possibility. We have had occasion to introduce the needle into subjects in whom the anatomy was grossly obscured by an enlarged thyroid gland, without difficulty or sequelae. In several patients the puncture was repeated without incident. In one case, postmortem examination of the larynx twenty-four hours following cricoid puncture indicated that there was only negligible

Fig. 5. Bronchiectasis. Right anterior oblique projection, both sides filled. Transcricoid bronchogram outlining severe tubular bronchiectasis in basal segments of right lower lobe. Adenolectasis and bronchiolectasis also demonstrated. Note position of needle in subglottic space.

trauma to the cricothyroid membrane and overlying tissue. Neck pain, swelling, or dysphonia seldom occur.

Over 200 cricothyroid punctures have been carried out by surgeons interested in the instillation of a respiratory tract detergent in the prevention of atelectasis in postoperative patients (7). They recorded 2 complications. In addition, Wilson (8) performed transtracheal anesthesia in 250 cases, using a 16- or 17-gauge plastic needle, with no complications. Harken and Salzberg (9) reported 1,000 cases with 3 minor complications during anesthesia for bronchoscopy by means of the transtracheal route, using an 18-gauge needle. Adriani and Parmley (10) had 2 complications in 350 instillations: one of deep cellulitis of the neck, and one in which the 25-gauge needle broke.

The amount of anesthetic required is strikingly less than that used when intubation is attempted. The more direct and consequently more effective anesthesia, plus elimination of the irritating transglottic

Fig. 6. Anteroposterior projection, right side filled. Large emphysematous bullous cysts with secondary deformity and displacement of bronchi. Note contracted right hemithorax with herniation of a portion of the left lung across the superior mediastinum.

catheter, results in studies of consistently better quality. The use of the puncture method in all age groups, including children and debilitated elderly people, has been recorded (4). Vickers (6) in England uses the procedure for ill or unconscious patients in whom intubation would be impossible or undesirable.

CONCLUSIONS

A transcricoid needle puncture technic was used for bronchography in 42 cases. The frequency and seriousness of the complications of this procedure appear to have been exaggerated in the past. With absorbable contrast media, antibiotic control, and careful attention to asepsis, the method appears to be safe, effective, and time-saving. It is particularly suited for departments of radiology in large and busy general hospitals.

ADDENDUM

Since submitting this paper for publication, 43 additional studies have been performed with one minor complication. A case of subcutaneous emphysema of the neck was discovered on a routine twenty-four-hour post-drainage study. This patient had no clinical complaints. This brings the total to 85 cases studied in the last twelve months.

St. Luke's Hospital
Amsterdam Ave. and 113th St.
New York 25, N. Y.

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SUMMARIO IN INTERLINGUA

Bronchographia Percutanee a Punctura del Membrana Crico-Thyroide

Un technica a punctura de agulia percutanee transcricoide esseva usate per le autores in 42 casos consecutive de bronchographia. Le methodo se ha provate salve, economic in tempore, practic, e efficace. Solmente tres complicationes esseva incontrate. Duo de istos esseva minor e esseva directemente relationate al procedimento usate mesme: Le occurrentia de un emphysema subcutanee que se acclarava promptemente sin tractamento e un episodio transiente de raucitate del voce. In le tertie caso, hemoptysis de grados sever occurreva; sed isto, apparentemente, non esseva relationate con le examine.

Previe objectiones contra le methodo es in grande mesura rendite invalide per le uso de un absorbibile substantia de contrasto, un control antibiotic, e un meticulose attention prestate al desiderato de asepsis.

Le efficacia de iste technica in provider detaliate informationes anatomic in statos normal e pathologic es demonstrate per un numero de bronchogrammas. Le methodo es particularmente adaptabile al uso in departimentos radiologic de grande e affairate hospitales general.

Radiographic Determination of the Rate of Bone Healing[1]

GEORGE P. VOSE, M.S., PAULINE BEERY MACK, Ph.D., SIDNEY O. BROWN, Ph.D., and AMMON B. MEDLEN, Ph.D.

THE HEALING of injured bone is a highly complex process, and its rate is affected by many variables, including diet, environment, and pathologic condition of the individual. The present study was undertaken in order to develop a radiographic method for determining the healing rate of injured bone. The radiographic approach seemed desirable since it would permit following bone repair in the same animal on a day-by-day basis.

Our initial attempts to measure the healing rate of fractured femurs of rats were unsuccessful because of uncontrolled displacement of the bone fragments. In addition, bone splints were destroyed by the animals in spite of all practical precautions. Success was greater when the tibia was substituted for the femur because the fibula served as a natural splint. A method was selected, however, which had been described by Haggar, Kinney, and Kaufman (1), who produced uniform lesions in comparative studies of bone healing in stained sections. In their method a longitudinal cut was made through the cortex of the anterior surface of the tibia with a rotary saw. In the resulting wound the intact bone required no splint, and highly uniform injuries were produced.

EXPERIMENTAL PROCEDURE

It can be demonstrated clearly that changes in bone mineral content can be recorded on an x-ray film. Methods for determining bone mineral *in vivo* from radiographs have been investigated by the authors for a number of years, using the densitometric approach (2–5). Virtama (9) has substituted a method for determining the emulsion silver in the radiograph in place of the densitometric system. Recently Omnell (6) applied a densitometric radiographic method for measuring repair of experimental injury in the interalveolar bone septa of dogs.

Since the theoretical aspects have been described previously (2, 10), these will not be considered extensively in this paper. It will be sufficient to say that the radiant power of an x-ray beam decreases exponentially in accordance with (*a*) the thickness of material penetrated, (*b*) its absorption coefficient, and (*c*) the energy of the beam. In the present work the energy of the beam was constant at 46 kvp with 1.0 mm. aluminum filtration. The absorption coefficient of bone, however, varied in accordance with its organic-inorganic ratio at each healing stage, and its cross-sectional volume increased as the bone grew.

Since the precise composition of the bone at each healing stage is complicated by organized hematoma and newly formed fibrous connective tissue, it was not practical to calculate its mass absorption coefficient at each testing period. Hence quantitative determinations of bone mineral were not made in this study, since the x-ray attenuation was governed by a number of components having different absorption coefficients. One possibility for gauging the rate of bone healing radiographically would be to obtain the aluminum equivalency for the lesion at each healing stage. This method was not feasible, however, because bone growth progressed throughout the study, and periosteal addition on the opposite side of the bone could not be distinguished from new bone in the healing lesion. Instead, it appeared feasible to compare the aluminum equivalency of the lesion with the

[1] From the Nelda Childers Stark Laboratory for Human Nutrition Research, Texas Woman's University, Denton, Texas, and the Radiation Biology Laboratory, Texas A. and M. College, College Station, Texas. Accepted for publication in October 1960.

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aluminum equivalency of adjacent non-injured cortical bone. On this basis, bone repair was considered to be complete when the absorbency ratio of the injured site to its control site regained its original value, or the value which pertained immediately before the injury.

The foregoing assumption depends, of course, on the constant composition of healing bone. Although electron microscopic and x-ray diffraction studies have shown no differences in crystalline structure between old and new bone, the matrix in newly formed bone shows a faster turnover rate with radioisotopes and generally exhibits more chemical reactivity. A possible interpretation is that these differences are due to physical forces such as the proximity to blood vessels or other variations in organic matrix composition (7). In order to check the effect of possible differences in x-ray absorption between equal masses of moisture-free new and old bone, sections of each kind weighing 0.25 mg. were removed from a healing rat tibia and radiographed. No measurable difference in x-ray absorption, as determined densitometrically, between the two kinds of osseous tissue was found.

Bone Wounding Method: For producing uniform bone lesions in the present study, Haggar's method (1) was used with only slight alteration. Fifty-two 100-day-old male albino rats of the Holtzman strain were anesthetized, and the rear right tibia was radiographed in a postero-anterior projection. Immediately thereafter the hair was clipped from the leg and the skin was bathed with a 2 per cent Roccal solution. The anterior surface of the tibia was exposed by a sharp skin incision approximately 1.5 cm. in length. Next, a longitudinal saw cut was made through the anterior cortex in the midportion of each tibia by an electric saw, the rotary cutter measuring 19 mm. in diameter and 1.6 mm. in width. Since the surrounding intact bone served as a natural splint, no displacement during healing could occur at the operative site. The skin incisions were sutured with Nylon thread, size 000, and covered with a layer of 1 per cent collodion. To prevent postoperative infection, each animal was injected intraperitoneally with 250 units of penicillin.

Fig. 1. Radiographic view of the bone lesion after seven days of healing.

Radiographic and Densitometric Procedures: Postero-anterior radiographs were made of the right tibia of each rat immediately before and following bone injury, again at three days, and, with the exception of the eighth week, weekly thereafter for a total of eleven weeks. During the course of the study, 3 animals were sacrificed at each testing period for histologic examination. Therefore, only 13 of the original 52 rats were radiographed at the terminal eleven-week testing period.

Figure 1 shows the site of the lesion after seven days of healing. The radiographs were made on Eastman Type AA film in cardboard exposure holders, at 46 kvp, 15 ma, one second, at a 20-inch focal-film distance. Since both the aluminum standardizing wedge and bones were of relatively small mass, this exposure technic produced radiographs having essential photographic linearity. Each ra-

diograph was made in a lead-lined exposure cabinet in which the anesthetized rat could be observed through a lead-glass window. A General Electric Model 90 x-ray head was mounted permanently at the top of the cabinet. The films were processed in Eastman solutions with constant agitation to assure even surface development, at 68° F.

The radiographs were evaluated in a specially constructed densitometric assembly described in previous reports (4, 5). The instrument is capable of correcting nonlinear H & D photographic curves to linearity by use of a tapped slidewire having a variable resistance throughout its length. Replicas of the resulting bone scans and their aluminum wedge equivalencies are shown in the accompanying sequence diagram (Fig. 2). In practice, three scans of 1.3 mm. thickness were made, crossing the lesion tangential to its longitudinal axis.

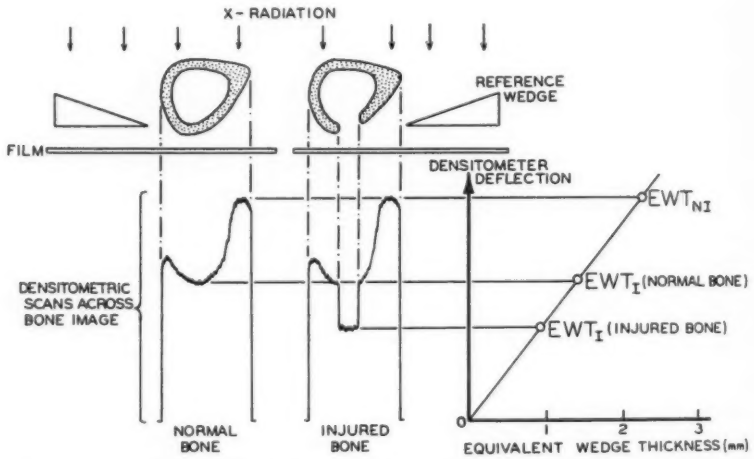

Fig. 2. Diagrammatic representation of radiographic method, showing densitometer deflections from radiographs of the bone plotted as a function of equivalent wedge thickness.

RESULTS

The rate of bone healing as determined by the densitometric method is shown graphically in Figure 3. Each point on the graph indicates the ratio of the equivalent aluminum wedge thickness of the incised bone (EWT_I) to the equivalent wedge thickness of adjacent nonincised bone (EWT_{NI}) for the test day indicated. Initial radiographs were made of each rat, the tibia was then injured as described, and a second radiograph was taken immediately. The sharp decrease in the aluminum equivalency ratio on the graph indicates the removal of bone by the rotary saw. Three days later a slight increase in absorptive material can be noted. The increase in bone density progressed less and less rapidly through succeeding weekly tests, but at the end of seventy-seven days it had regained its original value. At the seventy-seven-day testing period, therefore, the method indicated that the lesion had been filled completely with new bone and the bone had resumed its original proportions.

Figure 4 shows the degree of bone repair in two, five, ten, and twenty days. Almost no osteogenic tissue is visible in the lesion at two days, while at five days some subperiosteal osteogenic tissue is beginning to fill the gap. At ten days, only the midpoint of the lesion remains unfilled; and at twenty days the lesion is nearly filled with internal callus.

Figure 5, taken fifty days after injury, compares the interior wall of the healing cortex of an injured tibia with the same site

in a noninjured tibia. While the normal cortex is composed of compact bone, the honeycomb-like trabeculae in the partially healed lesion indicate that compact bone has yet to be formed. However, at seventy-seven days all of the internal callus had been resorbed and only slight irregularity in surface contour of the bone marked the site of the old lesion.

In order to evaluate the process of bone repair at different stages, histologic sections through the lesions were prepared with Lillie's silver impregnation method. The

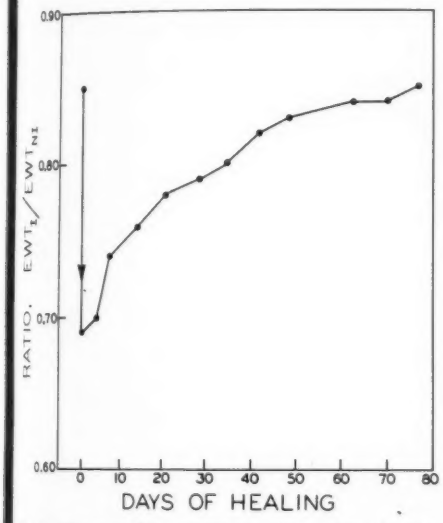

Fig. 3. The rate of bone repair as determined densitometrically from radiographs.

healing rate indicated by the sections shown in Figure 6 are in good agreement with the healing rate as determined by the radiographic method: By the third day after wounding, small flakes of osteogenic tissue appear within the bone marrow. At seven days, the connective tissue has a strong attachment to the bone at both the exterior and incised surface and is continuous with connective tissue in the bone marrow. Organized spicules of osteogenic tissue are present in the bone marrow, forming a bridge to support the free ends of incised bone. At forty-nine days a bridge of fairly compact bone has formed across the original lesion, and the quantity

Fig. 4. Comparative degrees of bone repair in two, five, ten, and twenty days.

of osteogenic tissue in the bone marrow has decreased. At seventy days the lesion is completely bridged by new bone and the cortical thickness is almost normal.

DISCUSSION

Since the shaft of a long bone grows concurrently both in width and length, the size variable must be considered in time studies involving bone absorptiometry. The tibia grows in length both at the distal and proximal epiphyseal plate regions. Hence, during the seventy-seven-day course of the study, the distance from the lesion to either end of the bone was increasing and, because callus deposition tended to obscure the lesion quite rapidly, it became increasingly difficult to determine its location on the radiographs of partially healed tibias. Since the injury was located between the zones of endochondral ossification, however, the distance between the fibula junction and the lesion remained constant. Therefore, that distance was measured on the film made immediately following bone injury and was used throughout the testing period. In this manner the precise location of the same

tracing paths across the lesion at each testing period was assured.

In the modeling processes affecting lateral bone growth, new bone is deposited in the periosteal region of long bones, and marrow erosion occurs within the medullary cavity. Therefore, during the seventy-seven-day course of the study the cross-sectional areas of the shaft represented by the and wall thickness of the tibia at the center of the lesion showed that changes in size during the seventy-seven-day period were less than 4 per cent. Moreover, the accuracy of the measurement was increased by the use of a ratio of x-ray absorption by two sites within the same bone instead of the actual absorbence of the healing lesion.

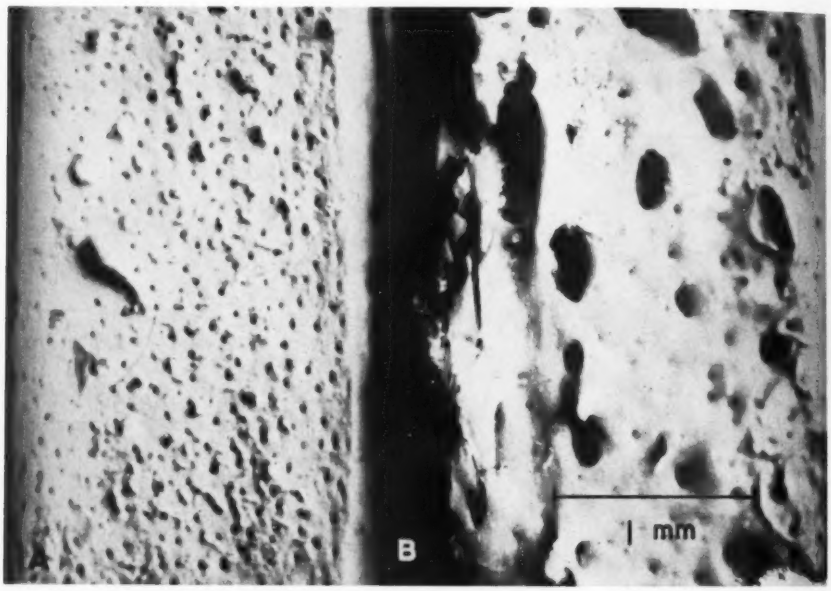

Fig. 5. A. Interior cortex of normal noninjured tibia. B. Same site in the injured bone after fifty days of healing.

densitometric scans of the bone image were increasing in size at the same time that the lesion was healing. The growth factor is further complicated by the failure of bone growth to proceed outward from a common central axis at equal rates. Tomlin, Henry, and Kon (8) found that the diameter of the rat femur increased by complete remodeling of the posterior wall as a result of endosteal resorption of its original cortex, while on the anterior surface the original cortex was retained but was eventually covered by periosteal and endosteal new bone. This effect might introduce errors if substantial growth occurred at the site examined during the seventy-seven-day test period. However, measurements of the cross-sectional width

The absorption characteristics of the overlying soft tissue may vary in accordance with the degree of healing of the skin incision over the bone lesion. Variations of soft-tissue components such as water or chondroitin sulfate might affect the x-ray absorption coefficient of the tissue as a whole. Since the absorption coefficient of soft tissue is approximately 50 per cent less than that of cortical bone (at the wave length used), the small thickness of tissue normally overlying the lesion could be doubled with a change in the mean absorption coefficient of bone plus soft tissue of about 3.5 per cent. This error is reduced further because (*a*) the skin incision and bone lesion are not directly superimposed when the leg is placed in a

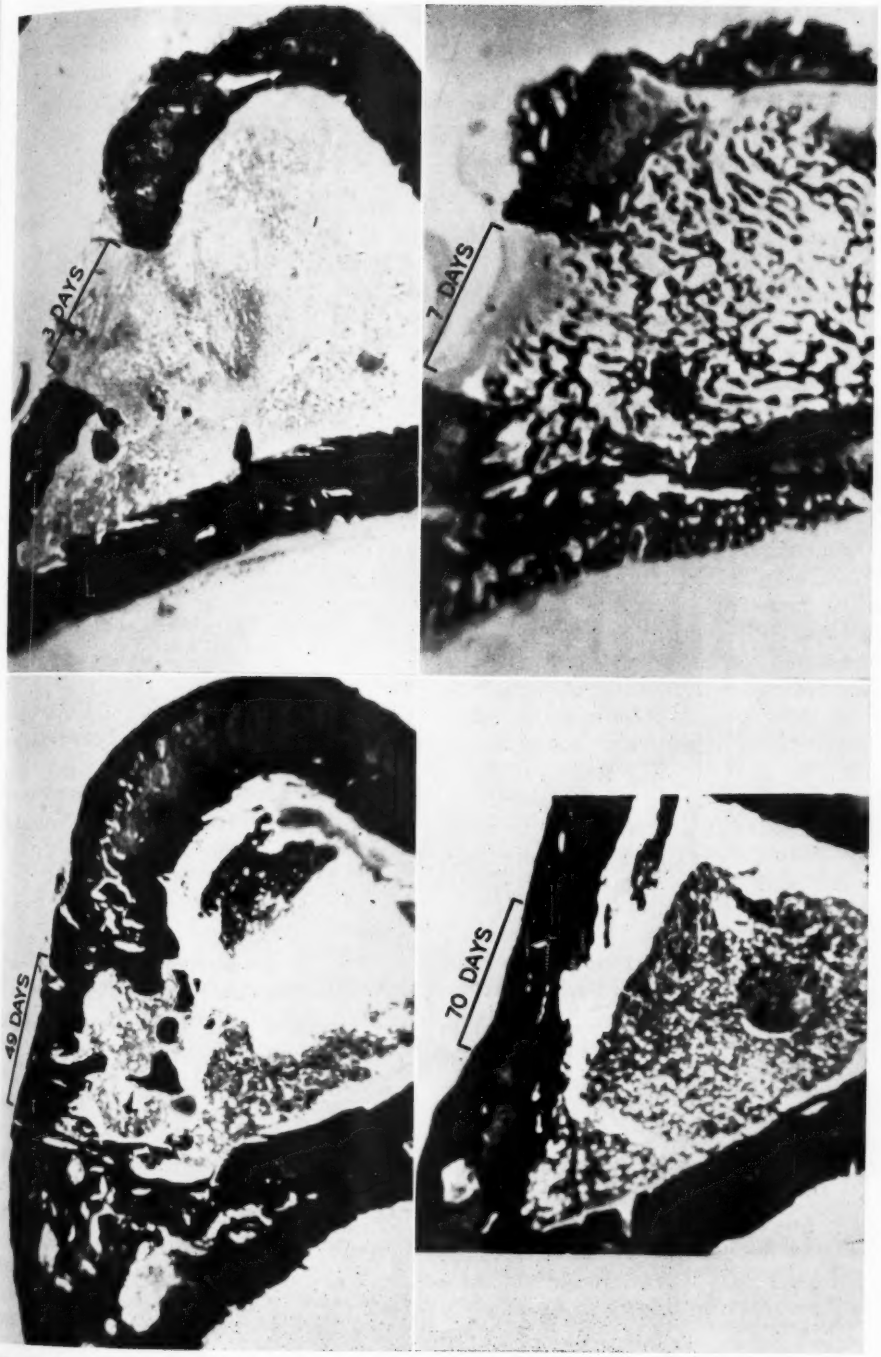

Fig. 6. Transverse sections through the bone lesion at three, seven, forty-nine, and seventy days of healing.

normal postero-anterior position on the radiographic film, and (*b*) any swelling of the tissue would be distributed fairly equally over both the lesion and the adjoining non-injured control bone. In any event, the skin incision healed at a much faster rate than the bone lesion, so that changes in the absorption characteristics of the soft tissue would be of relatively brief duration.

SUMMARY

A radiographic method for determining the rate of bone healing is described. This approach permits the following of bone repair in the same animal on a day-by-day basis. Uniform lesions were produced in the tibias of albino rats, and periodic radiographs were evaluated densitometrically to determine the rate of deposition of new bone. In the type of lesion described, complete remodeling occurred in seventy-seven days.

Transverse sections, prepared with the silver impregnation method of Lillie, indicated a close agreement between the usual histologic technic and the radiographic method.

The method appears to have useful applications in studies involving the effects of diet or environment on the healing rate of injured bone.

ACKNOWLEDGMENTS: The authors are deeply indebted to Jelle DeBoer, Gertrud Adam, and B. J. Stoner for technical assistance in the conduct of this study.

Nelda Childers Stark Laboratory
Texas Woman's University
Denton, Texas

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SUMMARIO IN INTERLINGUA

Determination Radiographic del Progresso de Resanation de Osso

Es describite un methodo radiographic pro determinar le progresso de resanation in osso. Le methodo permitte le observation de die in die del reparo de osso in le mesme animal.

Lesiones uniforme esseva producite in le tibias de rattos albin, e radiographias periodic esseva evalutate densitometricamente pro determinar le rapiditate del deposition de osso nove. Refaction complete del osso occurreva intra septanta-septe dies, e solmente un leve irregularitate in le contorno del osso marcava le sito.

Sectiones transverse, preparate per le methodo de Lillie a impregnation con argento indicava un stricte congruitate inter le usual technica histologic e le presente technica radiographic.

Le methodo pare haber utile applicationes in studios concernite con le effectos del dieta o del milieu super le progresso del resanation de lesionate ossos.

Right Renal Enlargements Causing Alterations in the Descending Duodenum

A Radiographic Demonstration[1]

IRWIN BLUTH, M.D.,[2] and PETER VITALE, M.D.[3]

FOR SOME TIME the senior author has been aware that many radiologists and clinicians in the allied fields of urology and gastroenterology do not realize that enlargement of the right kidney may produce deformity, displacement, or distortion of the descending duodenum. This fact is emphasized by the paucity of reports of such effects in the radiological literature and the failure of the major textbooks of roentgen diagnosis, gastroenterology, and urology to demonstrate them.

With the excellent methods now available for direct investigation of the upper urinary tract, it might seem superfluous to attempt to diagnose right renal enlargement from a gastrointestinal series. On the other hand, it should be recalled that many persons with renal disease present themselves with symptoms which seem to arise from the digestive tract (1). For a variety of reasons an enlarged right kidney may not be palpable on physical examination and may thus be overlooked. In such an event a careful investigation directed toward the gastrointestinal tract by an informed radiologist may detect the true nature of the ailment.

Anatomically the descending or second portion of the duodenum is from 7 to 10 cm. long, extending from the neck of the gallbladder, at the level of the first lumbar vertebra, along the right side of the spinal column as low as the upper border of the body of the fourth lumbar vertebra. The relation of this segment to the common bile duct and head of the pancreas has received much attention by radiologists investigating pancreatic disease. Posteriorly the descending portion of the duodenum is extraperitoneal and bears a variable relationship to the medial portion of the anterior aspect of the right kidney in the neighborhood of the hilus. It is connected with the kidney by loose areolar tissue. The variability of the relationship is indicated by the fact that not all the alterations in the appearance of the descending duodenum in our cases have been due to masses in the medial portion of the lower pole of the right kidney; further substantiation of this variation is afforded by 2 reports in the literature with roentgenograms demonstrating displacement of the descending duodenum by right adrenal gland enlargements (2, 3).

The basis of this paper is a series of 6 cases, collected over a seven-year period at the Beth-El Hospital (Brooklyn, N. Y.), in which masses involving various portions of the right kidney produced changes in the roentgen appearance of the descending duodenum. In 1 case a clear-cell carcinoma removed more than a decade prior to the last gastrointestinal series recurred locally, causing a large polypoid defect in the duodenum. In a second case a large cyst of the right kidney produced a smooth, concave, sharply demarcated anterior displacement of the descending duodenum. In a third case a mass at the lower pole of the right kidney did not displace the duodenum, but there was a clearly demarcated extrinsic pressure defect on its lateral aspect. In 2 patients with renal masses, the right lateral view during the gastrointestinal series revealed a marked anterior duodenal displacement. Sheinmel and Mednick (4), in 1951, made a valuable contribution to the radiographic investigation of the retroperitoneal area when they established values for the linear measurements of the

[1] From Beth-El Hospital, Brooklyn, N. Y. Accepted for publication in November 1960.

[2] Attending Radiologist, Beth-El Hospital; Clinical Instructor, Radiology, State University of New York, Downstate Medical Center, Brooklyn, N. Y.

[3] Resident, Radiology, Beth-El Hospital.

Fig. 1. Case I: A right lateral view of the upper gastrointestinal tract on July 23, 1956. There is a large intraluminal polypoid mass in the upper two thirds of the descending duodenum. The lesion obviously involves the posterior wall. This finding was confirmed at surgery.

Fig. 2. Case I: A right lateral view of the upper gastrointestinal tract on May 10, 1955 (fourteen months prior to Fig. 1). There is no evidence of any abnormality in the descending duodenum.

normal retrogastric and retroduodenal spaces. Yet, in their cases with anterior displacement of the duodenum, they do not include right renal enlargement as one of the causes. Beranbaum and Jacobson (5) discuss right renal enlargements with reference to duodenal displacement, but present only 1 such case in their paper. Mitchell and Sennott (6) describe a case of anterior displacement of the duodenum by a polycystic kidney. Ganem *et al.* (2) report anterior displacement of the duodenum by an adrenal carcinoma. In the sixth case in the present series a very large mass in the right kidney displaced the duodenum from its normal position so that it overlay the spine and also produced a considerable anterior dislocation.

CASE I: B. S., a 66-year-old white woman, entered Beth-El Hospital for the second time on July 19, 1956, with severe pain in the abdomen localized to the right upper quadrant. She had lost about 50 pounds during the three years prior to her admission. She had had a complete right nephrectomy in May 1943, at which time a clear-cell carcinoma was found.

Roentgenographic Findings: Beyond the bulb, in the second portion of the duodenum, was a large filling defect with polypoid components and extrinsic compression of the more distal portion. This intraluminal mass also appeared to have a large intramural component (Fig. 1). It might be noted that a gastrointestinal series done in May 1955 apparently did not show the duodenal defect (Fig. 2).

Surgery: On Aug. 1, 1956, an exploratory laparotomy was performed, showing a "retroperitoneal mass in the right upper quadrant which pushed the duodenum anteriorly and appeared to invade the posterior wall of the duodenum."

Pathology: The biopsy specimen showed metastatic carcinoma to the liver histologically compatible with a primary kidney carcinoma.

Discussion: This case probably represents a very rare series of circumstances. A right kidney with clear-cell carcinoma was removed in 1943 and in 1956 there was a local recurrence of the disease with liver metastases. The direct invasion of the descending duodenum by the recurrent tumor is highly unusual.

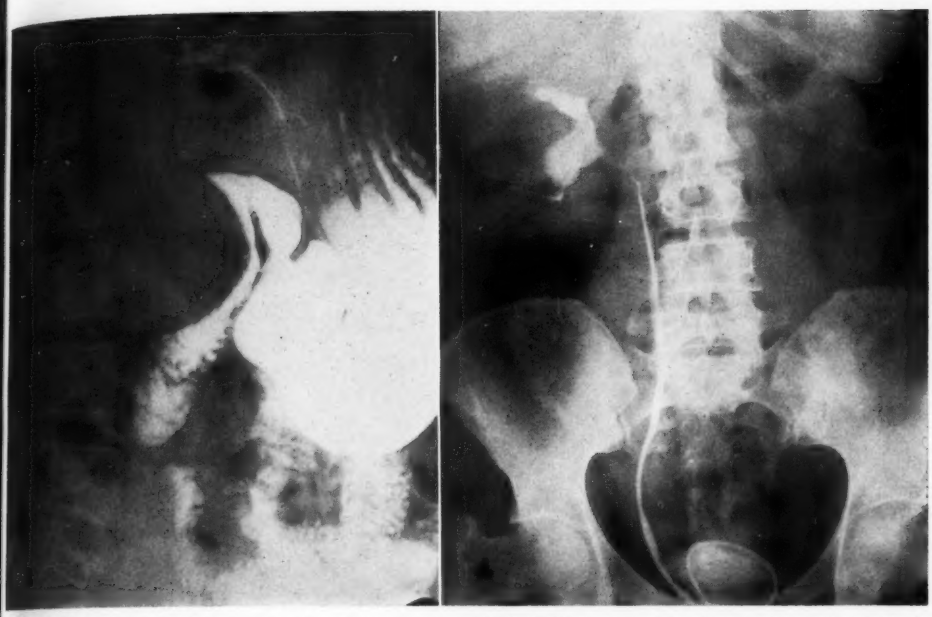


Fig. 3. Case II: A right lateral view of the upper gastrointestinal tract, March 26, 1953. An extrinsic defect on the posterior superior aspect of the descending duodenum is apparent.

Fig. 4. Case II: A right retrograde pyelogram made March 30, showing an enlarged right kidney. There is some dilatation of the pelvis and upper and middle calyces. The middle calyceal system shows a medial displacement. The pathologist reported multiple cysts of the right kidney.

CASE II: F. H., a 52-year-old white woman, entered Beth-El Hospital on March 22, 1953, complaining of pain in the right side of the abdomen and vomiting.

Roentgenographic Findings: A gastrointestinal series showed the descending duodenum to be displaced forward by a mass in the retroperitoneal region (Fig. 3). Intravenous urography demonstrated an enlarged right kidney. The outer half of this kidney and part of the superior half were involved by a mass which displaced the renal pelvis and calyces medially. The superior calyx was displaced downward. A retrograde pyelogram of the right kidney also showed medial displacement of the pelvis and calyces in the midportion by a mass at the upper half of the kidney. The superior calyx was rotated downward (Fig. 4).

Surgery: On March 31, a right nephrectomy was performed. The right kidney was found to be in its normal position. Its "upper two-thirds consisted of polycystic masses while the lower pole had the appearance of normal kidney."

Pathology: The surgical specimen consisted of a right kidney measuring 10 × 8 × 3 cm. On one side was a translucent cystic mass measuring 6 cm. in its greatest diameter. On section, this cyst was found to contain about 15 c.c. of clear fluid. The pelvis and ureters were normal. The remainder of the specimen was cystic and contained several cavities of different sizes, all lined by a smooth whitish tissue.

Diagnosis: Multiple cysts of the right kidney.

Discussion: The descending duodenum showed a very sharply demarcated extrinsic pressure defect on the upper part of the descending duodenum. The intravenous pyelogram revealed the abnormalities within the right kidney.

CASE III: T. L., a 65-year-old white woman, was admitted to Beth-El Hospital on Sept. 14, 1958, because of weight loss, dyspepsia, and substernal pain.

Roentgenographic Findings: A gastrointestinal series showed on the postero-anterior view an extrinsic pressure defect in the lateral aspect of the descending duodenum (Fig. 5) with questionable pressure on the posterior aspect as seen on the right lateral projection (Fig. 6). An intravenous urogram showed the right kidney to be enlarged, extending downward below the crest of the ileum. The lower half of this kidney appeared lobulated laterally. A concavity and pressure defect were present on the inferior calyx, the middle portion of which appeared indistinct (Fig. 7).

Surgery: On Sept. 30, 1958, a right nephrectomy was performed.

Pathology: The surgical specimen consisted of a

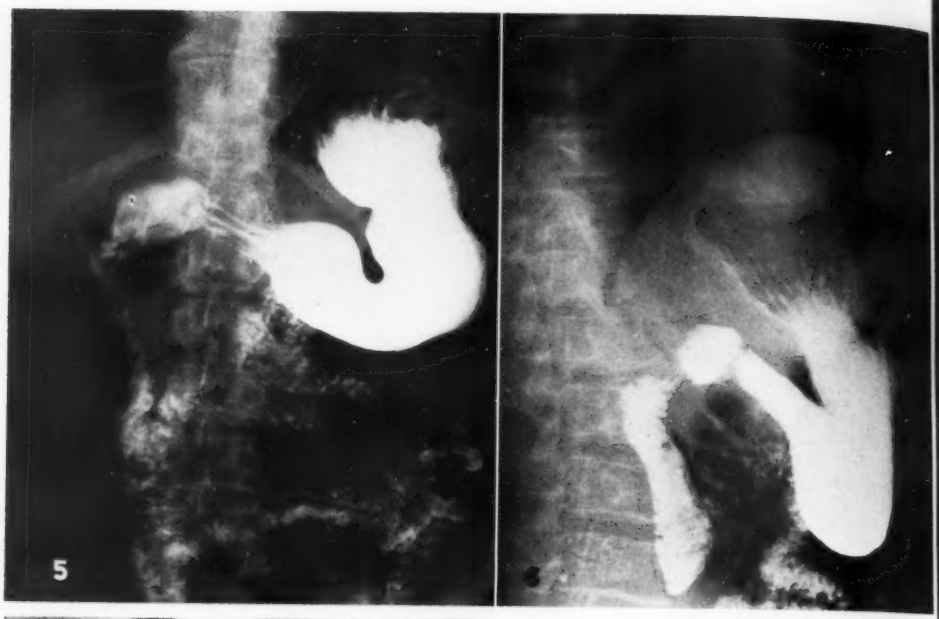


Fig. 5. Case III: Postero-anterior view of the upper gastrointestinal tract, Sept. 17, 1958, revealing a rather subtle concavity along the lateral border of the descending duodenum. There can be recognized an adjacent mass whose medial border seems to correspond with the concavity produced on the duodenum.

Fig. 6. Case III: Right lateral view of the upper gastrointestinal tract on the same date, showing no anterior displacement of the duodenum. The slight concavity on the posterior surface of the duodenum is a normal variant.

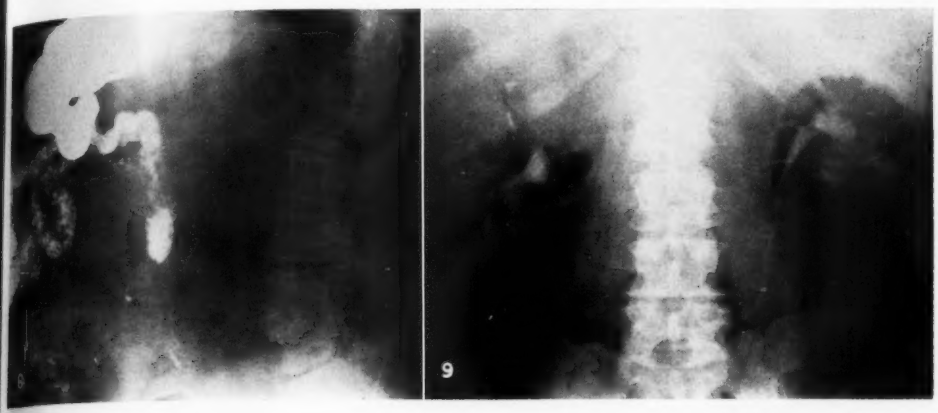
Fig. 7. Case III: The upper urinary tracts thirty minutes after the intravenous injection of Hypaque (Sept. 22, 1958). There is a mass at the lower pole of the right kidney which spreads the lower and middle calyceal segments. Pathologic examination revealed a clear-cell carcinoma of the lower pole of the right kidney.

right kidney weighing 335 grams. The serosa was smooth and glistening except at one pole, where there was a large tumor measuring 6 × 7 cm. which was firm and adherent to perirenal fat. At the other pole of the kidney was a well demarcated cystic cavity measuring 8 mm. and containing a clear yellow fluid.

Diagnosis: Clear-cell carcinoma of right kidney.

Discussion: The mass in the lower pole of the right kidney produced a lateral duodenal indentation. There was no anterior displacement, as the lesion was not situated behind the duodenum. This case illustrates the anatomical variation of the relationship between the right kidney and the duodenum. The kidney mass occupied the lower pole, including the medial segment, yet there was no effect on the posterior duodenum, classically described as overlying this portion of the kidney.

CASE IV: I. R., a 52-year-old white female, was admitted to Beth-El Hospital on Jan. 2, 1956, with a history of itching of the external genitalia for about three months prior to admission and a weight loss of 15 pounds despite apparent overeating.



Roentgenographic Findings: The gastrointestinal series revealed marked displacement of the duodenal curve anteriorly by a retroduodenal mass which was believed to be the right kidney (Fig. 8). An intravenous pyelogram showed the right kidney to be enlarged with a pressure defect between the middle and superior calyces laterally and anteriorly (Fig. 9).

Surgery: On Jan. 19, 1956, a right nephrectomy was performed, after a protruding mass had been found on the anterior surface of the kidney.

Pathology: The surgical specimen consisted of a right kidney measuring 13 × 8 × 9 cm. Projecting from the anterior mid and lateral surfaces was a well encapsulated, mottled, whitish-gray mass 6 cm. in diameter. Section revealed a lobulated tumor in the midportion of the kidney parenchyma, extending from the renal pelvis to the renal capsule.

Diagnosis: Clear-cell carcinoma of the right kidney with secondary carcinoma in a lymph node. Incidentally, the patient returned in 1957 because of a bleeding duodenal ulcer. The right lateral prone view of the upper gastrointestinal tract showed the descending duodenum now in its normal position (Fig. 10).

Fig. 8. Case IV: The right lateral view of the upper gastrointestinal tract in January 1956, revealing a very marked uniform displacement of the descending duodenum.

Fig. 9. Case IV: Five-minute film after intravenous injection of Hypaque. There is a mass at the lateral aspect of the right kidney, displacing the middle calyx downward and the upper calyx medially. The pathologist's report identified this lesion as a clear-cell carcinoma.

Fig. 10. Case IV: A right lateral view of the upper gastrointestinal tract one year after right nephrectomy. The descending duodenum is now seen to be in its normal position.

Discussion: In the light of the patient's complaints and physical findings, the discovery of the right renal tumor was accidental. The right lateral view of the upper gastrointestinal tract showed a marked anterior displacement of the entire descending duodenum. This type of defect corresponds well with the defects shown in Sheinmel and Mednick's paper, in which they illustrate the effects of enlarged retroperitoneal lymph nodes. The same projection of the gastrointestinal tract made one year later showed the duodenum in its proper location for this obese patient.

CASE V: F. F., a 58-year-old white woman, entered Beth-El Hospital for the first time on March 11, 1958, with low-back pains.

Roentgenographic Findings: In a gastrointestinal series the duodenal bulb and curve were well outlined and no intrinsic defects were demonstrated, but there was a marked anterior displacement of the descending duodenal loop by a large retroperitoneal mass (Fig. 11). Intravenous urography showed the right kidney to be greatly enlarged. There was evidence of a pressure defect causing downward displacement of the pelvis and calyceal system ascribable to a

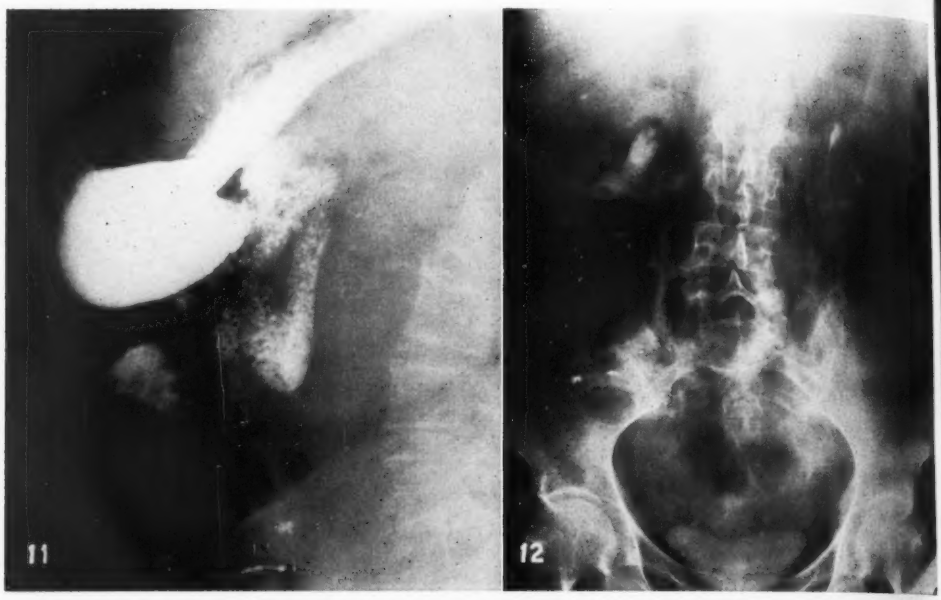


Fig. 11. Case V: A right lateral view of the upper gastrointestinal tract revealing significant anterior displacement of the entire descending duodenum. An enlarged right kidney soft-tissue shadow can be seen.

Fig. 12. Case V: Fifteen-minute film made after intravenous administration of Hypaque, showing marked distortion of the pelvis and calyces on the right side. The left renal shadow appears enlarged. The patient left the hospital before a histologic diagnosis was established.

space-occupying mass within the upper pole (Fig. 12). The left kidney appeared enlarged. Further investigation and possible surgical intervention were planned, but the patient discharged herself on March 31, 1958, and unfortunately no further information could be obtained.

Discussion: This case also demonstrates significant anterior displacement of the entire duodenum by an enlarged right kidney. This was confirmed by the intravenous pyelogram, but there is no histologic diagnosis.

CASE VI: S. K., a 72-year-old white man, was admitted to Beth-El Hospital for the first time on March 3, 1960, complaining of pain on the right side of the abdomen and swelling in the same area.

Roentgenographic Findings: Intravenous urography revealed a normal left kidney. On the right side a large mass extended below the level of the iliac crest. Its relationship to the kidney could not be established, as there was no excretion of the contrast medium on this side. A gastrointestinal series showed a hiatus hernia about the size of a small orange. The duodenal bulb appeared normal but the duodenal curve was displaced across the midline so that the descending limb lay over the spinous processes of the vertebrae rather than to the right of them (Fig. 13). Lateral and oblique views showed displacement of the bulb anteriorly by an enormous retroperitoneal mass (Fig. 14). The extent of the mass was apparent on the one-hour film (Fig. 15). A right retrograde pyelogram revealed the effect of the mass on the proximal part of the right ureter and the dilatation of the calyces (Fig. 16).

Surgery: On March 21, 1960, an exploratory laparotomy was done, disclosing a "tremendous tumor mass involving the entire right kidney, filling out the entire right upper quadrant retroperitoneally and pushing the bowel down anteriorly and laterally to the opposite side." The mass extended down into the pelvis and surrounded part of the inferior vena cava and abdominal aorta. The entire bulk of the tumor and right kidney was removed except for a portion which was found to have already invaded the lumen of the vena cava.

Pathology: The surgical specimen consisted of a right kidney measuring 25 × 15 × 10 cm. The external surface was irregular and lobulated. On section the mass consisted of a soft yellow and brown tissue with hemorrhagic areas. On the anterior surface of the mass was an attenuated, elongated, crescentic area of tannish tissue which was normal kidney. The pelvis and upper calyx were moderately dilated. The renal vein was entirely filled with necrotic tumor tissue.

Diagnosis: Clear-cell carcinoma of right kidney.

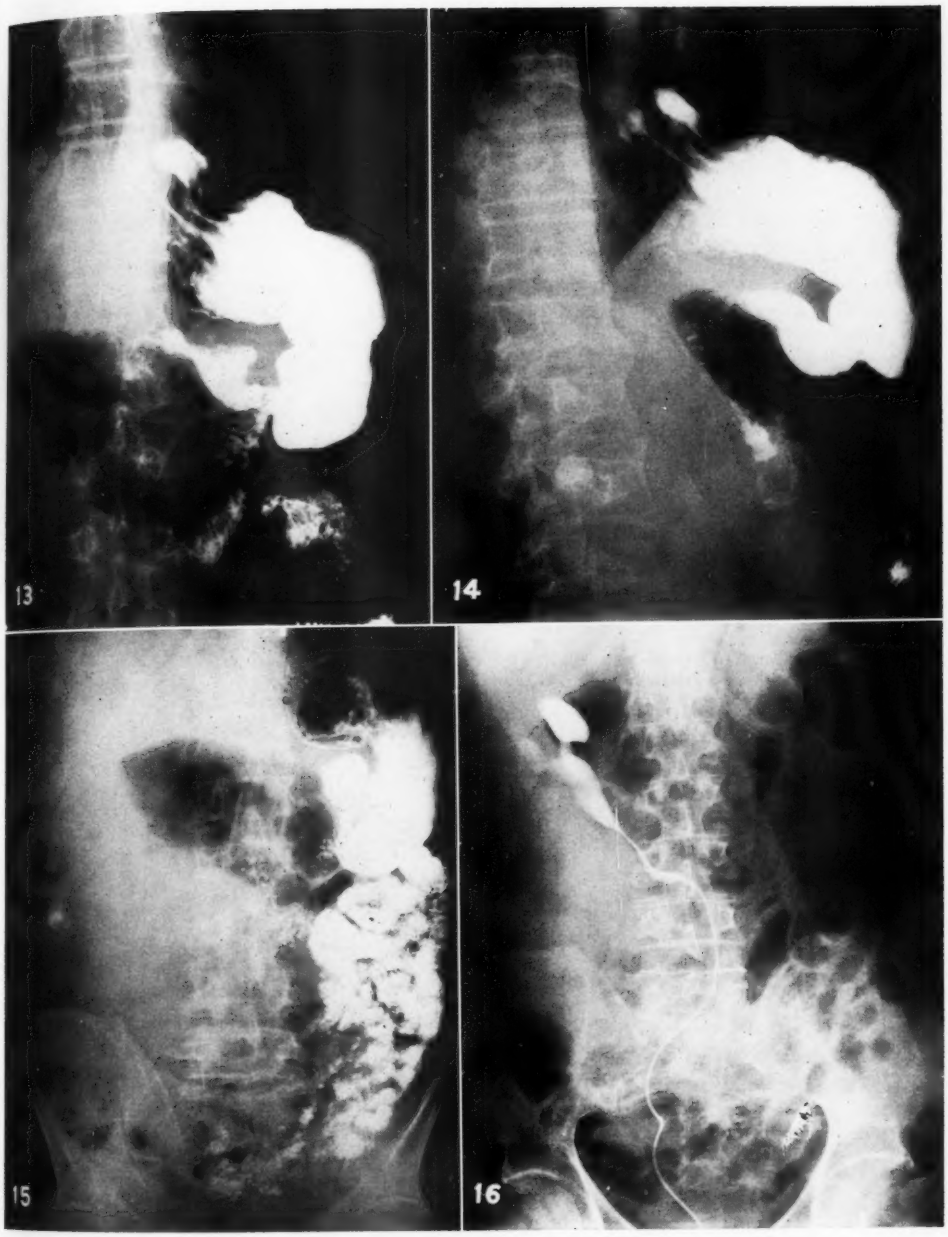


Fig. 13. Case VI: Postero-anterior projection of the upper gastrointestinal tract. Note the position of the descending duodenum overlying the lumbar vertebrae rather than to their right. There is a hiatus hernia.

Fig. 14. Case VI: Right anterior oblique view. Note the marked anterior displacement of the descending duodenum.

Fig. 15. Case VI: Prone film one hour after the beginning of the barium meal study. The extent of the mass in the right side of the abdomen is clearly seen. Note the displacement of the small intestine, which is crowded into the left abdominal quadrants.

Fig. 16. Case VI: A right retrograde pyelogram revealing a dilated pelvis and calyces as well as multiple extrinsic defects and displacement of the ureter. At surgery this enormous mass was found to occupy the kidney. The histologic diagnosis was clear-cell carcinoma.

Discussion: In this case the difficulty lay in the proper identification of an obvious mass in the right side of the abdomen. Eventually the diagnosis of carcinoma of the kidney was established by nephrectomy and pathological determination. Although renal tumors seldom reach the size seen in this instance, the effect produced on the descending duodenum was quite dramatic.

SUMMARY

The fact that enlargements of the right kidney can produce changes in the roentgen appearance of the descending duodenum is pointed out and demonstrated by 6 cases. The anatomical relationships of the right kidney and descending duodenum were reviewed and the variability of this relationship is indicated.

In the six cases reported, several positive findings involving the descending duodenum were illustrated: (*a*) direct invasion by a malignant renal tumor; (*b*) a sharply demarcated localized indentation on the posterior surface; (*c*) a lateral indentation; (*d*) a generalized anterior displacement; (*e*) a displacement across the midline.

Beth-El Hospital
Rockaway Parkway and Linden Blvd.
Brooklyn 12, N. Y.

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SUMMARIO IN INTERLINGUA

Allargamentos Dextero-Renal Como Causa de Alterationes in le Duodeno Descendente

Un Demonstration Radiographic

Es signalate le facto que allargamento del ren al latere dextere pote esser le causa de alterationes del apparentia roentgenologic del duodeno descendente. Le facto es demonstrate in 6 casos. Le relationes anatomic inter le ren al latere dextere e le duodeno descendente es revistate. Le variabilitate de iste relationes es indicate.

In le sex casos reportate, plure constatationes positive concernente le duodeno descendente es illustrate: (a) Un invasion directe per un maligne tumor renal; (b) un acutemente demarcate indentation localisate al superficie posterior; (c) un indentation lateral; (d) un generalisate displaciamento anterior; e (e) un displaciamento a transverso le linea central.

Intramural Hematoma of the Jejunum

A Case Report[1]

GORDON J. CULVER, M.D., HERBERT S. PIRSON, M.D., ELMER MILCH, M.D., LEONARD BERMAN, M.D., and F. JORGE ABRANTES, M.D.

TWO OF THE authors recently published an article on intramural hematoma of the duodenum (7) in which the literature on this condition was reviewed and a case was reported. Shortly after the appearance of this article an opportunity arose to examine a patient with an intramural hematoma of the jejunum. Intramural hematoma is more rarely seen in the jejunum than in the duodenum, and it seemed worthwhile to report this example, since there were roentgenographic changes which made it possible to establish the diagnosis preoperatively.

CASE REPORT

C. F., a 52-year-old man, was admitted to The Buffalo General Hospital, Feb. 22, 1960, complaining of abdominal pain, nausea, and vomiting of about five days duration. The pain was crampy in nature at the onset, gradually developing into a generalized abdominal discomfort. The nausea and vomiting became less severe and were accompanied by abdominal distention. Nine weeks prior to the present admission, the patient had a coronary thrombosis and anticoagulant (Dicumarol) therapy was started. Four weeks later he experienced sudden lower abdominal pain, crampy in nature, which recurred several times in the course of the next few days, accompanied by constipation. He was hospitalized in another institution and

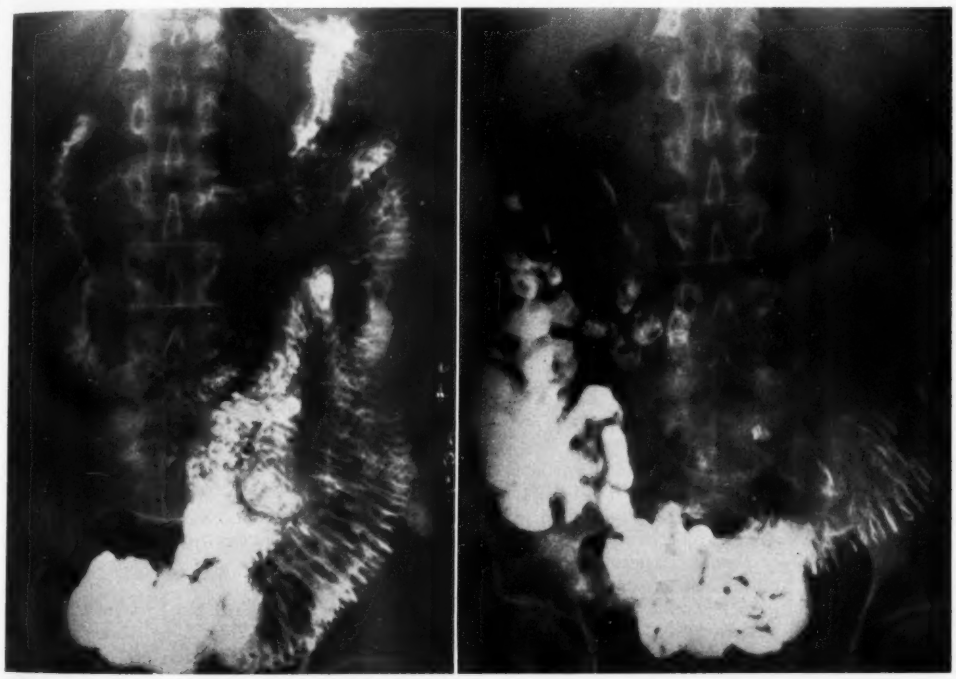

Fig. 1. Films from small-bowel series, showing dilatation from the ligament of Treitz down, to involve a considerable part of the jejunum. A large intramural mass extends throughout the distended jejunum, with crowding together of the valvulae conniventes producing a coil-spring appearance.

[1] From the Department of Radiology and Surgery of the University of Buffalo, and the Radiology Department of The Buffalo General Hospital, Buffalo, N. Y. Accepted for publication in November 1960.

Fig. 2. A film taken from a small-bowel series six months following surgery, demonstrating considerable reabsorption of the hematoma.

Dicumarol was discontinued. Laxatives and bed rest relieved the pain. Prior to admission to The Buffalo General Hospital, anticoagulant therapy had again been started.

On admission to The Buffalo General Hospital, the patient's temperature was 98.6° F., pulse 116, blood pressure 130/92, respirations 24. He appeared acutely ill and markedly dehydrated. The abdomen was moderately distended, somewhat tense, and diffusely tender. There was rebound tenderness. Peristaltic sounds were absent. On rectal examination, tarry stool was found. The rest of the physical findings were essentially within normal limits. Hemoglobin was 14.0 gm., and the white blood count 18,000, with 6 per cent band forms, 72 per cent filaments, 15 per cent lymphocytes, and 7 per cent monocytes. The urine was cloudy, with a specific gravity of 1.023, negative for sugar, protein +, containing 40 to 60 red blood cells. The blood urea nitrogen was 26, total proteins 5.9 (albumin 4.2, globulin 1.7), Na 145, K 4.6, Cl 89, CO_2 15.1; bleeding time two minutes, clotting time three minutes, and prothrombin time "over two minutes."

A Cantor tube was inserted and hydration was started. At this time the gastrointestinal bleeding was attributed to hypoprothrombinemia. Vitamin K_1 oxide (Mephyton) was administered intravenously, bringing the prothrombin time down to sixteen seconds. Conservative therapy was continued, with improvement of the clinical picture: progressive relief of abdominal pain, decrease of distention, and return of peristalsis. The hemoglobin was 10.3 gm. on the third day and 8.2 gm. on the fourth day. The Cantor tube was removed, and oral feedings were started. To correct the blood loss, 1,500 c.c. of blood was given. The patient improved following transfusions which

Fig. 3. Photograph taken at surgery, showing intramural hematoma involving the wall of the entire jejunum, which was markedly thickened and edematous, but without obstruction.

raised the hemoglobin to 12.4 gm. A barium-enema examination was negative. This was followed by an upper gastrointestinal and small-bowel series.

The upper gastrointestinal series showed no abnormalities in the esophagus, stomach, or duodenum. There was dilatation of the jejunum for a considerable portion of its extent, involving several loops from the ligament of Treitz down. What appeared to be a large intramural mass extended throughout the distended jejunum, with crowding together of the valvulae conniventes, producing a coil-spring appearance. There was no obstruction, and barium passed through the small bowel in a normal time. The ileum showed an essentially normal mucous-membrane pattern without dilatation. A radiographic diagnosis of "intramural infiltrating process of the jejunum, probably hematoma," was made.

In view of the possibility of a small-bowel cancer (*vs.* an intramural hematoma), an exploratory laparotomy was performed. On opening the abdomen, old blood was found free in the peritoneal cavity. An intramural hematoma involved the

wall of the entire jejunum, which was markedly thickened and edematous but without obstruction. This hemorrhage involved the mesentery of the jejunum down to the insertion in the posterior abdominal wall. Five hundred cubic centimeters of blood were removed from the peritoneal cavity.

Following this operation, the patient recovered, with no complications, and was discharged on the eighth postoperative day. On a three-month follow-up he was asymptomatic, with no evidence of obstruction.

DISCUSSION

Gastrointestinal and peritoneal bleeding have long been known to be complications of anticoagulant therapy. Numerous reports are found in the literature (1, 17).

In 1952 Berman and Mainella (4) reported the case of a 69-year-old woman who exhibited a picture of small-bowel obstruction during the course of anticoagulant therapy (Dicumarol) for coronary disease. She did not have gastrointestinal bleeding, but the operation disclosed an intramural hematoma of the terminal ileum. Similar cases have since been reported by Pearson and MacKenzie (20) and Groch *et al.* (12).

In the case recorded above, symptoms of small bowel obstruction were followed by melena and paralytic ileus, with signs of peritoneal irritation. Later secondary anemia developed. The condition was attributed to Dicumarol therapy and x-ray studies demonstrated an intramural hematoma of the proximal jejunum.

Reports of intramural hematoma of the bowel were found infrequently in the literature until 1954, when emphasis was placed upon the subject by Felson and Levin (8). In 1957, Spencer *et al.* (25), reviewing the English literature, found 33 such cases and added 1 of their own. Twenty-one cases have since been reported, making a total of 55. Of these, more than half were in the duodenum, 15 in the jejunum and duodenojejunal bend, and the remainder were equally divided among the ileum, cecum, colon, and sigmoid. In the majority of cases trauma was the etiologic factor. Rarely were blood dyscrasias reported as the cause of this condition, and in several instances, no cause was mentioned. Possenti (23) reports a case of hematoma of the terminal ileum which he attributed to surgical trauma during reduction of an intussusception.

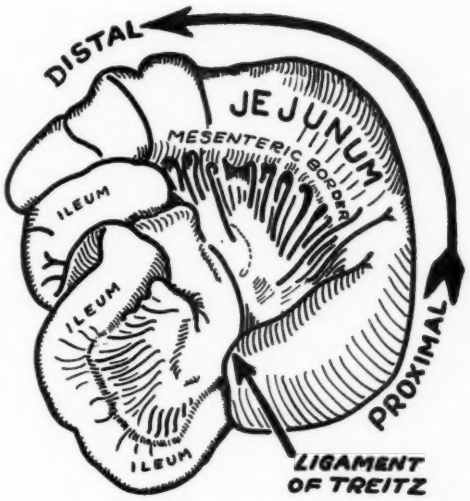

Fig. 4. Diagram showing the relationship of the jejunum and ileum in the photograph reproduced in Fig. 3. The jejunum has been placed over the stomach for better visualization.

An intramural intestinal hematoma should be suspected after careful history taking and physical examination. In the majority of the cases x-rays will demonstrate the lesion. In 8 previous cases the roentgenologic diagnosis was made prior to definite therapy (7, 8, 14, 17, 19, 21, 22, 27).

Roentgen diagnosis of intramural hematoma of the jejunum is based on the same appearance that was first described by Felson and Levin (8) for intramural hematoma of the duodenum. This consists of evidence of an intramural mass associated with crowding together of the valvulae conniventes, producing a coil-spring appearance.

The common treatment of this condition has been evacuation of duodenal hematomas and resection of the involved loop for hematomas of other segments of the intestine. Conservative treatment (nasogastric suction, fluids, blood transfusion) has been used occasionally with good results (8, 15, 18, 22). However, in many of the operated cases conservative treat-

ment was tried for periods of variable length with no remission of symptoms.

Although no long-term follow-up studies have been reported, conservative therapy should be tried first. In the case reported here, films taken after six months demonstrate considerable reabsorption of the hematoma. Only long-term follow-up studies, however, will indicate whether scarring and narrowing of the lumen of the bowel will take place, with the establishment of obstructive symptoms.

SUMMARY

A case of intramural hematoma of the jejunum is reported. This was found to be caused by Dicumarol therapy and was diagnosed preoperatively from the roentgenograms. The clinical and radiologic findings are discussed. Etiology, diagnosis, and treatment are reviewed.

The Buffalo General Hospital
100 High Street
Buffalo, N. Y.

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SUMMARIO IN INTERLINGUA

Hematoma Intramural del Jejuno: Reporto de un Caso

Es reportate un caso de hematoma intramural del jejuno, in un patiente qui habeva essite sub tractamento anticoagulante (con Dicumarol) pro un thrombosis coronari. Le condition esseva diagnosticate ante le operation a base de roentgenogrammas. A causa del possibilitate de cancere (contrastate con hematoma), laparotomia exploratori esseva effectuate, e le diagnose roentgenologic esseva confirmate. Sanguine esseva removite ab le cavitate peritonee, e le patiente se restabliva satisfactorimente. Tres menses plus tarde ille esseva asymptomatic e sin signo de obstruction.

Le constationes roentgenologic consiste de evidentia de un massa intramural, associate con compression del valvulas connivente (a apparentia de un resorto spiral).

Duplication of the Stomach

A Case Report[1]

R. JOHN GOULD, M.D.,[2] and ALLAN H TOFFLER, M.D.[3]

DUPLICATIONS of the alimentary canal are uncommon congenital errors of development, most frequently encountered in the pediatric age group. They may be found anywhere from the base of the tongue to the rectum, the most common site being the small intestine (1).

Anatomically, true duplications occur as tubular or spherical hollow structures which are almost always intimately attached to the normal alimentary tract along the mesenteric border. A well defined coat of smooth muscle is always present, and, when the attachment is firm, this coat is shared with the muscularis of the normal viscus. Duplications are always lined with epithelium that resembles some portion of the gastrointestinal tract, but at any particular level the lining mucosa of the duplicate structure may be quite different from that of the normal bowel to which it is attached. For example, colonic mucosa may line a duplication of the esophagus. A communication may exist between the duplicate and the normal lumen, but the most common method of presentation is as a blind pouch attached to a portion of the normal intestinal tract (2). The non-communicating variety is usually filled with fluid, the nature of which depends on the type of lining cell.

Among all the duplications of the gastrointestinal tract, those involving the stomach are considered the most rare. The author of a recent report (3) found only 28 cases in the English literature. The following is a report of a congenital duplication of the stomach in an adult.

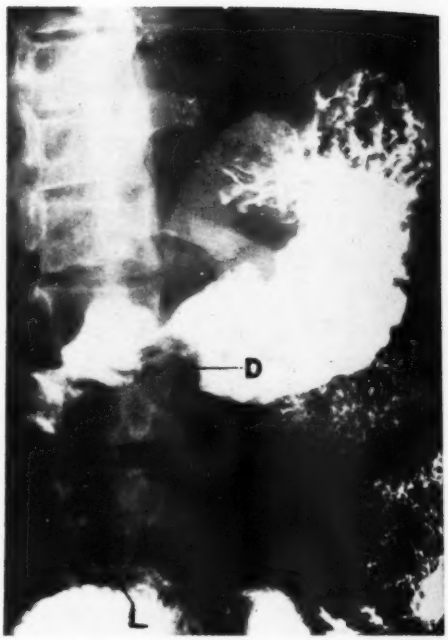

Fig. 1. Extrinsic pressure defect (D) in the antrum of the stomach and widened duodenal loop (L).

CASE REPORT

A 29-year-old white male was admitted to the U.S. Army Hospital, Fort George G. Meade, Md., in April 1959, complaining of epigastric pain of three to four months duration.

The patient was in excellent health until four months prior to admission, when he began to experience severe epigastric pain, usually relieved by milk and antacids and occasionally, but not always, related to meals. At that time the serum amylase was 92.5 Gomori units, the white blood count was 20,000 with a normal differential, and the hemoglobin and hematocrit were within normal limits. An upper gastrointestinal series revealed questionable scarring of the duodenal cap, definite widening of the duodenal loop, and the presence

[1] From the Department of Radiology, USA Hospital, Fort George G. Meade, Md. Accepted for publication in October 1960.

The opinions expressed herein are those of the authors and do not necessarily reflect the views of the U. S. Army.

[2] At present a Trainee, National Cancer Institute, and Chief Resident, Department of Radiology, Philadelphia General Hospital, Philadelphia, Pa.

[3] At present Clinical Fellow in Gastroenterology, Department of Internal Medicine, Yale University and Grace-New Haven Hospital, New Haven, Conn.

of a smooth filling defect on the greater curvature of the stomach in the region of the antrum (Fig. 1). After an interval of six weeks on a strict medical regime, including bland diet, antacids, and antispasmodics, a second gastrointestinal examination was performed. No abnormalities were noted in the duodenal bulb, but there was persistent widening of the duodenal loop with spasm and inflammatory changes in the second portion of the duodenum; a marked narrowing of the descending limb with distortion of the mucosal pattern had been present on the initial examination. Once again the smooth-walled filling defect indenting the greater curvature of the gastric antrum was noted.

The patient's symptoms of burning epigastric pain and left upper quadrant fullness were only partially relieved by treatment, and he was admitted to the hospital for a more complete evaluation.

The past medical history, family history, and review of systems were all non-contributory. On physical examination, all findings were within normal limits except for moderate epigastric and left upper quadrant tenderness. There was no palpable mass, abdominal rigidity, or rebound tenderness.

The blood count on admission showed 15,000 white cells, with 62 per cent neutrophils, 4 per cent band forms, 30 per cent lymphocytes, 4 per cent eosinophils; hemoglobin 15.7 gm.; hematocrit 52 per cent; sedimentation rate 22 mm. in an hour (Wintrobe). Urinalysis was normal. Fasting blood sugar, serum bilirubin, alkaline phosphatase, and blood urea nitrogen were all within normal limits. Stools were negative for occult blood, ova and parasites, and excess neutral fats. Serum amylase was 61 Gomori units; serum lipase 1.6 and 2.4 units (normal value less than 1.0 unit). A chest film, electrocardiogram, and gallbladder series were all within normal limits.

The patient remained afebrile during his entire course in the hospital. A diagnosis of chronic pancreatitis with pseudocyst formation was made in view of the elevated serum lipase and the gastrointestinal findings.

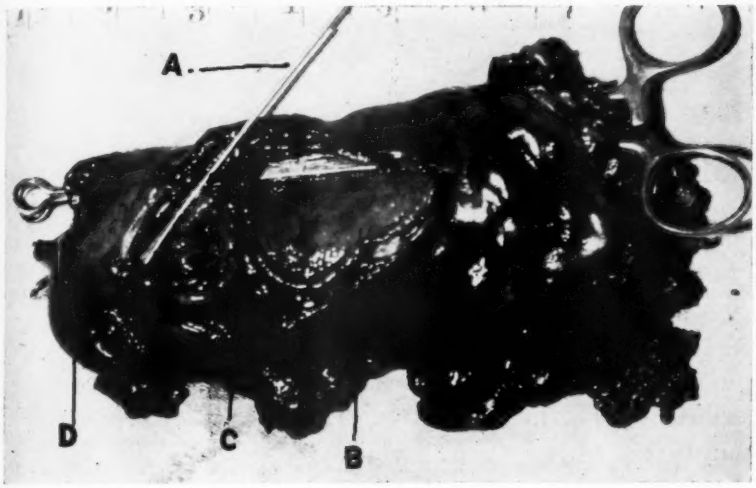

Fig. 2. Gross specimen. A. Probe in the duplication. B. Gastrostomy opening revealing normal gastric mucosa. C. Greater curvature. D. Pylorus.

Surgical exploration was undertaken and the head of the pancreas was found to be thickened, firm, and somewhat irregular. Near its superior portion a thick-walled cystic mass was palpated, in the wall of the gastric antrum along the greater curvature. A gastrotomy was done proximal to the "cyst," and the stomach lumen and lining mucosa were grossly normal. The cystic structure was easily palpated in the wall of the stomach and bulged into the lumen. There was no connection with the gastric cavity. The "cyst" was opened, and approximately an ounce of white viscid fluid was removed from it; it had a mucosal lining, but thorough exploration confirmed that it was a blind pouch with no communication with the gastric or duodenal lumen. Since it was so intimately attached to the stomach wall, no attempt was made to dissect it. The duodenum was fully mobilized and found to be normal, as were the gallbladder, common duct, and remainder of the small bowel. Because of the obvious close vascular relationship between the gastric antrum and the cyst, a subtotal gastrectomy was performed.

Pathologic Report: The gross specimen (Fig. 2) measured approximately 23 cm. along the greater curvature and 7 cm. along the lesser curvature. On the greater curvature was a separate cystic

Fig. 3. Low-power photomicrograph showing mucosa of the duplication (A), mucosa of the normal stomach (B), and the muscular wall shared by both. The duplication shows normal columnar gastric epithelium and typical gastric glands.

structure 4 × 5 cm. in diameter, lined with normal intact gastric mucosa but having no visible communication with the normal stomach. A small portion of normal appearing pancreas was attached to the pyloric end of the stomach. Another "cyst," 1 cm. in diameter, was found intramurally, just distal to the larger one, interposed between the pancreatic fragment and the normal gastric lumen. Histologic sections of the stomach showed both cystic structures to be lined with gastric mucosa, consisting of normal simple columnar gastric epithelium and gastric glands containing both chief cells and parietal cells. Smooth muscle composed the wall separating the stomach from the cyst, and the entire surgical specimen was covered by an intact serosa (Fig. 3).

The pathologic diagnosis was duplication of the stomach.

DISCUSSION

Embryology: Various theories have been advanced to explain the congenital origin of duplications of the alimentary tract. Lewis and Thyng (4) described multiple diverticula occurring normally on the antimesenteric surfaces of the gut in fetal pigs, rabbits, and human beings during the second month of gestation. Normally they disappear, but it is not unreasonable to consider the abnormal persistence of one or more of these fetal diverticula. If such a persistent diverticulum is restrained from growing externally by developing embryonic muscle layers, it is held closely proximate to the fetal gut and may well finally form an intra-intestinal cyst in the mature alimentary tract. However, if no such restraint is imposed, a mature congenital diverticulum is formed. In either case, the abnormal structure may or may not communicate with the normal bowel lumen and is usually found on the antimesenteric border of the gut.

Bremer (5) proposed a more anatomically correct approach. His observations in the six-week embryo pointed up the normal obliteration or narrowing of the fetal alimentary tract by the rapid overgrowth of the gastrointestinal tube at this

time, reflected in the rapid overgrowth of entodermal cells. A solid tube is formed, but this never extends for the entire length of the tract at one time. Shortly thereafter, long chains of fluid-filled vacuoles are seen forming in the solid masses of entodermal cells. Coalescence of these vacuoles with one another and the lumen of the intestinal tract re-establishes the internal continuity of the alimentary tube. Rarely, chains of coalesced vacuoles may not communicate with the reformed lumen, or may communicate at only one end of the chain. Continued growth and development of these "aberrant chains" will then form a second "gut" having all the components of the normal intestine.

The above discussion accounts rather adequately for duplications of tubular portions of the intestine. However, to explain a gastric duplication, Bremer had to invoke a second mechanism, as the stomach is not known to pass through a solid stage in the course of its development. During the second or third fetal month, the gastric lumen is narrowed to a dorsoventral slit, the walls being thrown into large folds, many of which approximate each other across the lumen. If a fusion occurs, producing an epithelial bridge, it is conceivable that the submucosa and growing gastric musculature may grow into this bridge to form a common wall between two separate portions of the stomach.

Clinical Findings: The clinical symptoms of a duplication of the alimentary tract are varied, depending on the size and location of the anomaly. The presenting complaints in duplications of the stomach are most often obstruction, ulceration and bleeding, epigastric pain, vomiting, and occasionally a palpable epigastric mass. Preoperative diagnosis is rare, but roentgen examination of the upper gastrointestinal tract with barium may offer a clue when a smooth-walled pressure defect is seen anywhere along the greater curvature of the stomach, particularly in the antral region. Where there is a communication of the duplication with the intestinal lumen, the ingested barium may outline the "extra" portion of the alimentary tract (6).

We believe that the symptoms in the present case were related to the very intimate association of the pancreas and the duplication. This probably resulted in mild obstructive factors in the adjacent pancreas with local regurgitation of pancreatic enzymes. This impression is borne out by the characteristic location of the pain and the elevated serum lipase values. Pathologic confirmation of pancreatitis is lacking, and it is presumed that a larger biopsy specimen would have contained areas of mild edematous pancreatitis.

Treatment: The treatment of choice is surgical excision of the duplication, the object being to remove as much as possible without sacrificing the integrity of the parent organ. When the duplicate structure is intimately associated with the normal organ, as in our case, excision entails resection of the duplication and the involved portion of the stomach and reestablishment of primary intestinal continuity. When total excision is not technically feasible, compromise procedures such as external marsupialization with destruction of the lining cyst membrane (7) or enteroenterostomy (8) may be employed.

SUMMARY

Duplication of the stomach is a rare congenital anomaly. An unusual case occurring in a young adult male is presented. The embryology, symptomatology, and treatment are briefly reviewed.

ACKNOWLEDGMENT: We wish to express our appreciation to Maj. Kenwyn Nelson, M.C., Chief of Surgical Service, U.S. Army Hospital, Fort Meade, Md., and to Capt. Lee Rosenblum, M.C., pathologist, Second Army Medical Laboratory, for their assistance in the preparation of this article.

Radium Clinic
Philadelphia General Hospital
Philadelphia 4, Penna.

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SUMMARIO IN INTERLINGUA

Duplication del Stomacho: Reporto de un Caso

Es reportate un caso de duplication del stomacho, constatate in un masculo de vinti-novem annos de etate. Le roentgenogrammas revelava un persistente allargamento del ansa duodenal e un defecto de replenation a contornos lisie que indentava le curvatura major del antro gastric. Al operation un massa cystic de crasse parietes esseva trovate intra le pariete del stomacho, con extrusion verso le interior sed sin communication in ille direction. Le "cyste" esseva revestite a su superficie interior de mucosa gastric.

Le symptomas in iste caso—principalmente dolores epigastric—esseva attribuite al intime association del duplication con le pancreas, lo que resultava probabilemente in factores levemente obstructive in le pancreas, con regurgitation local de enzyma pancreatic.

Es discutite le base embryologic del duplication.

The Radiographic Findings in Neurogenic Bladder[1]

RICHARD M. FRIEDENBERG, M.D., and CHARLES NEY, M.D.

NUMEROUS articles have documented the clinical symptomatology and the many causative factors associated with neurogenic lesions affecting the bladder, but the associated radiographic findings (1) have been infrequently and often incompletely presented. Among the more common causes of neurogenic bladder are such entities as trauma with damage to the spinal cord or cauda equina, congenital lesions such as spina bifida, multiple sclerosis, syphilis, diabetes mellitus, and neoplasm. The clinical picture varies, depending on the severity of the lesion and its level. In some cases there will be urinary retention with associated overflow incontinence. In other instances there may be total loss of urinary control, with inability to initiate or inhibit the stream, continuous dribbling, or involuntary evacuation of urine at regular intervals.

The radiographic findings associated with neurogenic bladder are caused directly by the neuromuscular effects of the neurogenic lesions on the bladder and sphincters and indirectly by the resulting obstruction. The roentgen picture is also altered by secondary infection and calculi formation.

RADIOGRAPHIC FINDINGS

The accompanying illustrations, selected from the cystourethrograms of 50 patients with neurogenic bladder, demonstrate the usual radiographic findings. The major abnormalities reflect changes in the shape, size, and position of the bladder, the configuration of the urethra, the status of the external urethral sphincter, and the competence of the ureteral orifices.

Figure 1 is the cystogram of a girl of three and a half years with neurogenic bladder resulting from lumbosacral spina bifida and posterior meningocele that had been repaired at three weeks of age. There

Fig. 1. Cystogram of a girl of three and a half years, illustrative of the large atonic bladder with ureteral reflux and deviation to the right.

is a large atonic bladder with bilateral vesico-ureteral reflux of such a degree as to make possible visualization of the entire excretory system of both kidneys. The bladder is deviated to the right. A funnel urethra is poorly demonstrated. This is an example of the less common large atonic neurogenic bladder with ureteral reflux and characteristically eccentric position (5).

Figure 2, the cystourethrogram of a 26-year-old male, shows a typical "hourglass" deformity following a traumatic cord lesion at L-1. Cystometry revealed hypertonicity of the bladder. The causes of the hourglass deformity are unknown, but it may result from asymmetrical innervation of the bladder secondary to the neuro-

[1] From the Departments of Radiology and Urology, Lebanon Hospital, Bronx, N. Y., and Grand Central Hospital, New York, N. Y. Accepted for publication in November 1960.

Fig. 2. Typical cystourethrogram of hourglass deformity following a cord lesion at L-1.

logic lesion, with a spastic muscular area causing the narrowing in the midportion. The trigone may be either above or below the indentation. There are bilateral ureteral reflux and a funnel urethra, just distal to which is a moderately spastic external sphincter.

The "pine-tree"-shaped bladder shown in Figure 3 is an unusual deformity of neurogenic origin. In this patient, an adult male, there was complete absence of the sacrum and coccyx, with a neurogenic lesion existing from birth. The cystometric reading showed the bladder to be hypertonic. The marginal sacculations are probably secondary to the obstructive phenomena as well as to the neurogenic lesion.

Another variant is the severely contracted hypertonic bladder shown in Figure 4. This resulted from a traumatic spinal cord lesion at T-7. The illustration shows the funnel urethra with dilatation of the external sphincter and minute sacculations of the bladder wall.

Fig. 3. The "pine-tree bladder," an unusual type of deformity associated with neurogenic lesions.

Fig. 4. Severely contracted hypertonic bladder due to cord trauma at T-7.

Figure 5 illustrates a common sequence. Following a traumatic lesion, at the level of L-3, there are seen a hypertonic bladder of fairly large size with deviation to the right, a well demarcated funnel urethra,

and a severely spastic external sphincter. These may be termed the semiclassical findings of neurogenic bladder.

Figure 6 shows a hypertonic neurogenic bladder secondary to a traumatic lesion at D-10. The marked dilatation of the external sphincter is not uncommonly associated with hypertonic bladders.

Fig. 5. Semiclassical findings of neurogenic bladder: hypertonic bladder of fairly large size, with deviation to the right; well demarcated funnel urethra; severely spastic external sphincter.

The neurogenic bladder shown in Figure 7, secondary to a traumatic lesion at C-7, presents a rare finding, namely, saccular dilatation of the posterior urethra. There is an associated spastic external urethral sphincter. The bladder is hypertonic in type and in the frontal projection was seen to be deviated to the right.

DISCUSSION

The effects of a neurogenic lesion on the urinary tract are often quite widespread and may appear unrelated. In order to understand the various manifestations, it was considered useful to describe the findings according to anatomical locations.

Fig. 6. Hypertonic neurogenic bladder secondary to a traumatic cord lesion at D-10.

The Bladder

Shape: The shape of the bladder varies widely, depending on many factors not clearly understood. It may be rounded or oval, smooth-walled, or irregular from trabeculations, cellules, saccules, and diverticula. "Pine-tree" and "hourglass" are descriptive terms applied to certain bladders, usually of the hypertonic type. The "pine-tree bladder" is wide at the base, gradually tapering as the dome is approached. Its outline is commonly serrated and irregular. This form is usually considered most characteristic of neurogenic bladders, but differentiation must be made from other conditions, especially patent urachus.

The term "hourglass bladder" has caused much confusion in the literature. It has been used in two senses: first, in a descriptive sense, applied to those bladders which give the appearance of an hourglass; secondly, as a definitive term limited to congenital lesions, the so-called true hourglass bladder. According to Zellermayer and Carlson (2), congenital hourglass bladders should be differentiated from (*a*)

Fig. 7. Saccular dilatation of the posterior urethra, an unusual finding in a neurogenic bladder secondary to trauma at C-7.

cord bladder with relaxation of the trigone (the neurogenic type), (*b*) congenital or acquired diverticula, (*c*) patent urachus, (*d*) vesica duplex or bipartita, (*e*) various other septal divisions, (*f*) constriction due to inflammatory conditions, (*g*) the effect of extrinsic or intrinsic injury, and (*h*) absence of the seminal vesicles and prostate, congenital or acquired. Cases of hypertrophy of the trigone resembling hourglass bladder have been reported (Young and Wesson, 3).

In any particular instance, the attempt to differentiate between congenital hourglass bladder and that due to other causes may be extremely difficult, if not impossible. In neurogenic bladders, for example, unless the patient had been studied prior to the neurogenic lesion, the exact cause of the hourglass appearance may not be ascertained. Caulk (4) believed that most hourglass bladders have a congenital basis in the form of pre-existing hypertrophic bands.

The trabeculations, cellules, saccules, and diverticula, which usually are not prominent, are the result of both obstruction and neurogenic factors.

Size: The size of the neurogenic bladder varies from a capacity of only a few cubic centimeters of urine to many liters. It will depend for the most part on the type and the level of the lesion in the central nervous system. The large atonic bladders are the result primarily of the lesion and secondarily of obstruction. The large hypertonic bladders are probably due entirely to the outlet obstruction, causing a gradual increase in residual urine.

Position: The frequency of lateral deviation of the bladder (approximately 64 per cent) in a recent evaluation of 50 patients with neurogenic bladder (5) is impressive. Most of the deviations were to the right. Change in position was not a direct result of bladder size but was thought to be due to an asymmetrical effect of the neurologic disturbance on the innervation of the bladder or of its supporting structures.

The Urethra

Funnel Urethra: The so-called funnel urethra is a dilatation of the prostatic urethra of the shape suggested by this designation. The wider portion is at the bladder neck, with gradual distal tapering. There has been a great difference of opinion as to the significance and cause of this phenomenon. A summary of the literature has been presented elsewhere (1, 6).

Saccular Dilatation of the Posterior Urethra: Saccular dilatation of the posterior urethra in neurogenic bladders is a rare observation (Fig. 7). In our review of the literature (1), we found no previous reference to this phenomenon. It may be related to funnel urethra, but it has a distinctive appearance, the dilatation being widest at the midportion of the posterior urethra rather than proximally. We have found this abnormality in hypertonic bladders only. Its rarity precludes any conclusions as to its cause.

External Urethral Sphincter

The Spastic External Sphincter: Spasticity of the external urethral sphincter

is not unusual in neurogenic bladders and may be suspected during the passage or withdrawal of a catheter. The external sphincter should be carefully studied with the panendoscope and by cystourethrography (Figs. 5 and 7) before the diagnosis is made. The use of the sphincterometer (7) may be an additional aid. In many instances the spasticity of the external sphincter does not prevent complete emptying of the bladder, but certainly it is the primary obstructing factor in some cases where emptying is incomplete. This latter conclusion was reached by the present authors in two ways: first, by careful study of cystourethrograms, especially of voiding and post-voiding films, where the contrast material was held in the region of the external sphincter and not at the bladder neck; second, by scrutiny of failures of transurethral resections of the internal sphincter.

Little attention has been paid this important problem. Emmett, Daut, and Dunn (8) offered two possible explanations for the spasticity of the external sphincter in neurogenic bladders; first, the increased tonicity may be a response to a lesion of the upper motor neuron; second, the extravesical spastic reflexes from the lower extremities and other muscles below the level of the lesion may be contributing factors. Langworthy *et al.* (9) in their textbook state: "If the cortico-spinal fibers are injured, the external sphincter of the bladder may share in the increased tone of other striated muscles of the body." Experimentally they found that stimulation of the pudendal nerves caused contraction of the external sphincter, which greatly increased the resistance of the urethra.

The Relaxed External Sphincter: Relaxation of the external sphincter (Figs. 4 and 6) is more common than one would gather from the literature. In 8 of our first 20 cases of traumatic lesions of the spinal cord, the external sphincters were relaxed. This condition was found in both flaccid and spastic cases and apparently was not related to the level of the lesion. In general, the volume of residual urine was small, but this was not invariably true as it amounted to 100 c.c. in one case, to 90 c.c. in another, and in still another to 210 c.c.

Emmett *et al.* have presented an excellent discussion of this problem, especially in relation to those cases with small residuals and incontinence.

Incompetence of Ureteral Orifices

Vesicoureteral reflux is an interesting phenomenon. It is visualized radiographically when contrast material is injected into the bladder through a suprapubic tube or the urethra and enters either or both ureters. Often, a complete retrograde ureteropyelogram (Figs. 1 and 2) may be obtained (10–15).

SUMMARY

The primary changes of neurogenic bladder demonstrable roentgenographically are those affecting the shape, size, and position of the bladder, configuration of the urethra, status of the external sphincter, and competence of the ureteral orifices. Characteristic cystourethrograms of patients with neurogenic bladder have been reproduced in an effort to familiarize the radiologist with the variations in the radiologic picture. The possible mechanisms from which the changes arise have been discussed.

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Lebanon Hospital
Grand Concourse and Mt. Eden Parkway
New York 57, N. Y.

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SUMMARIO IN INTERLINGUA

Le Constationes Radiographic in Casos de Vesica Neurogene

Le constatationes radiographic associate con vesica neurogene es describite e illustrate per urethrogrammas characteristic. Le vesica pote exhibir alterationes de conformation, dimension, et position. Le urethra pote esser infundibuliforme, o le urethra posterior pote exhibir un dilatation saccular—usualmente in le portion intermediari. Le orificios ureteral es incompetente e permitte le refluxo ureteral del substantia de contrasto injicite in le vesica.

Iste alterationes es causate directemente per le effectos neuromuscular del lesiones neurogene super le vesica e le sphincteres e indirectemente per le resultante obstruction. Le tableau roentgenographic es etiam alterate per infection secundari e per formation de calculos.

Oral Extrahepatic Cholangiography: A Simple Reliable Technic[1]

ALEX NORMAN, M.D., and MEHDI SAGHATOLESLAMI, M.D.

IN THE PAST twelve years, since the introduction of the triiodo contrast media for oral cholecystography and Cholografin for intravenous cholangiography, the accuracy of gallbladder examinations has increased strikingly. Criteria have been established which permit a more careful classification of gallbladder disease and a more precise localization of obstructive lesions.

As a result of the higher incidence of extrahepatic duct visualization, lesions about the ampulla of Vater and in the periductal region have entered the realm of x-ray diagnosis. A technic of oral cholecystography that will visualize the entire biliary system is therefore essential. An ideal study would require few films and no fluoroscopy; it should be accomplished in a minimum of time and follow a simple routine (14). Such a method has been evolved by us in the past six years.

The purpose of this presentation is primarily to demonstrate a technic of "complete" oral cholecystography with the aid of a synthetic cholagogue (Bilevac) and no adjuvant drugs either *per os* or intravenously, such as have been mentioned by many writers.

METHOD

A preliminary postero-anterior view of the right upper quadrant is obtained on the day prior to the study. The patient is instructed to have a fat meal for lunch but to restrict all fatty or fried foods at dinner. At 9 P.M. the contrast medium is taken in the usual manner. Telepaque is used in dosages of 3 to 6 grams, dependent upon the weight of the patient.

At 9 A.M. the following day, a postero-anterior and a right posterior oblique view of the gallbladder region are made. The supine view is most reliable and serves as a baseline of gallbladder volume study (contractility).

Fig. 1. Clear outline of cystic, common hepatic, and common ducts.

Following the fat meal, a single evacuation film is made at ten minutes, with the patient in the supine position rotated 15° onto the right side. In our experience the supine film taken ten minutes following the fat meal is most significant for "complete" oral cholecysto-cholangiography. Several authors have mentioned this view as an additional one but have not stressed its anatomic value in the examination (3–5, 15) (Figs. 1–4). Sachs (3) and Shehadi (5) speak of adding it to their routine but not to the exclusion of the conventional positions. Our reliance upon a single film in the supine position after the fatty meal has been so successful that rarely are the other technics as reviewed by Shapiro *et al.* (6) needed.

Anatomically and physiologically the supine (right posterior oblique) view of the gallbladder is correct. Because the cystic and common ducts assume a dependent position in relation to the gallbladder in the supine position, there is a better diffusion of the heavier bile-contrast medium toward the neck of the gallbladder and into the extrahepatic ducts (16). Another advan-

[1] From the Hospital for Joint Diseases, New York, N. Y. (A. N., Chief of Diagnostic Radiology; M. S., Resident in Radiology). Accepted for publication in November 1960.

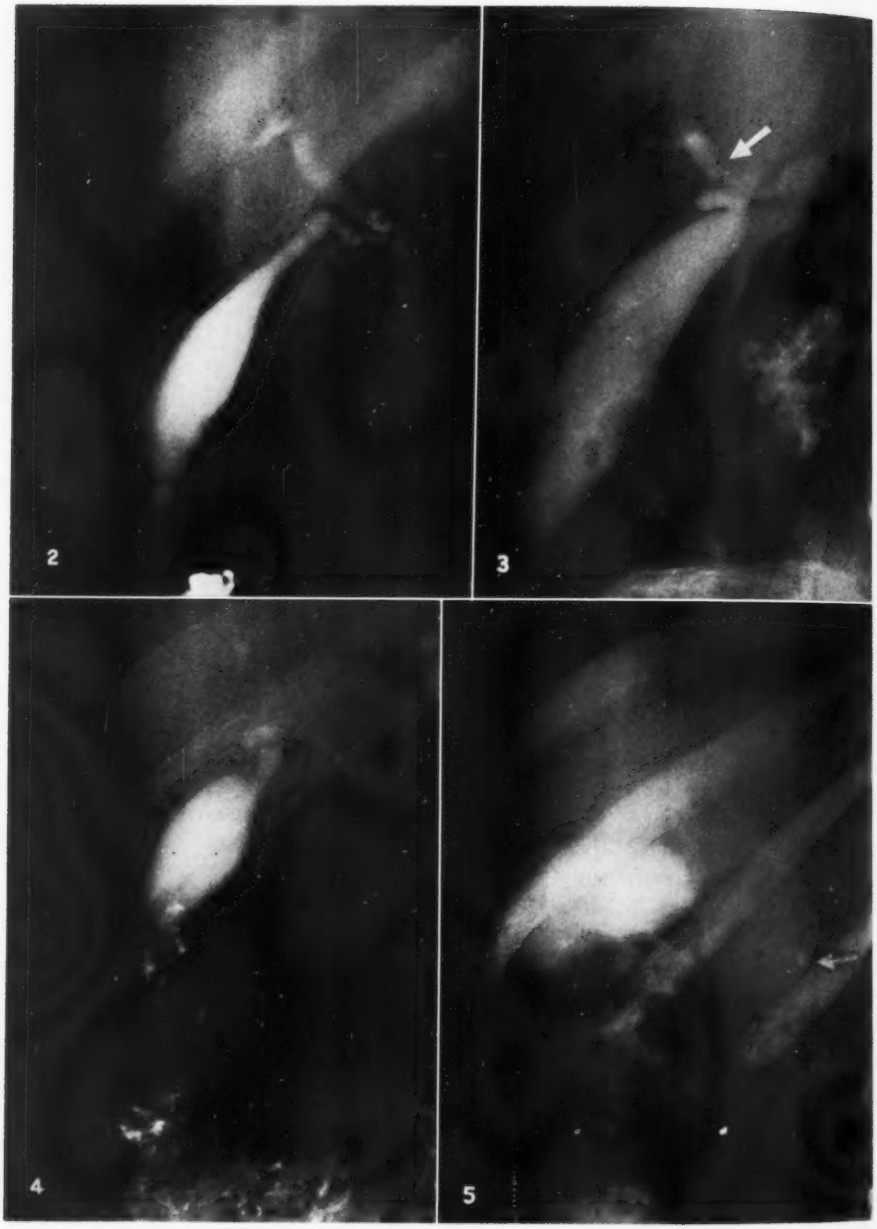

Fig. 2. Well demonstrated hepatic ducts.
Fig. 3. Excellent opacification of hepatic radicals and common hepatic duct.
Fig. 4. Complete outline of common duct to the ampulla.
Fig. 5. Calculus localized in the common duct by oral cholangiography.

tage of this position is escape of gas from the more dependent right colon toward the splenic flexure or distal colon. Artefacts are often eliminated, thereby increasing the accuracy of diagnosis without the aid of more complex methods such as laminag-

raphy, fluoroscopic spot-film examination, or repeat study. In addition, the right posterior oblique position will unfold the gallbladder and cystic duct, anatomically exposing the extrahepatic duct system.

Most important is the timing of the evacuation films. Much has been written about the physiology of emptying of the gallbladder and the influence of cholagogues. With the development of synthetic oral cholagogues, numerous authors arrived, by trial and error, at a "best time" interval after the fat meal. The optimum time has been determined as that in which there is evidence of decrease in gallbladder size and extrahepatic duct visualization. This has varied from five to thirty minutes after the fat meal (1, 3–5, 7–9). Much has been written about the value of cholecystokinin, Prostigmine 1:4,000, and Demerol for better demonstrating the ducts. We feel that these drugs are unnecessary.

After control observations of a large series of patients in whom exposures were made at five, ten, twenty, thirty, and forty-five minutes, we found the ten-minute supine film to be the best. In ten minutes the ducts are most clearly demonstrated and there is approximately 30 to 40 per cent reduction in gallbladder size. The common hepatic ducts are seen in addition to the cystic and common ducts in many instances.

DISCUSSION

Extrahepatic cholangiography is an essential part of each oral gallbladder examination. Completeness of examination can readily be accomplished by the simple technic described above.

Since Graham and Cole introduced oral cholecystography in 1924, great strides have been made in the diagnosis of biliary disease. However, not until the advent of the tri-iodo contrast media, did extrahepatic biliary duct demonstration become possible with reasonable frequency.

Prostigmine, cholecystokinin, morphine, Demerol, or other adjuvant therapy is unnecessary for extrahepatic duct visualization. This is borne out by the results

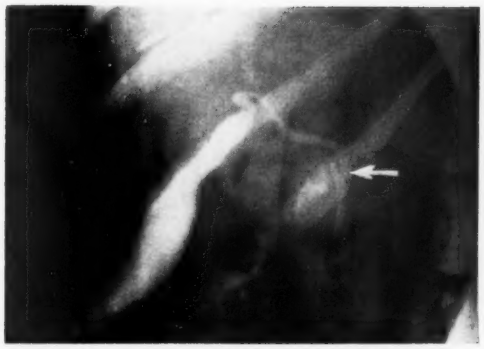

Fig. 6. Anatomic variation: medial insertion of the cystic duct.

of the simple method described. One hundred consecutive oral cholecystograms were reviewed; in 85 per cent of the cases in which the gallbladder was visualized, extrahepatic duct visualization was obtained on the single film taken ten minutes after the fatty meal. Our observations confirm those described by Feigelson (4), that the fatty meal is primarily of value not for determination of gallbladder contractibility but rather as a means of obtaining added information regarding the extrahepatic duct system.

Other authors who have evaluated visualization of the biliary duct report positive results varying from 5 per cent (11) to 75 (Sussman) and 80 per cent (Shehadi). Because of this wide variance in figures, we are thoroughly convinced that our method of examination was most important in acquiring the higher percentage of oral cholangiography. Sharpening the tools of technic is a prerequisite to diagnostic accuracy.

The importance of "complete oral cholecysto-cholangiography" in localizing calculi in the extrahepatic ducts is apparent (Fig. 5). Of equal value are: determination of anomalies of insertion of the cystic duct as an aid to the surgeon in his operative approach (Fig. 6); localization of obstruction in the biliary duct; evaluation of disease of the head of the pancreas, manifest by change in position of the lower end of the common duct; and lastly the defining of lesions about the

ampulla and second part of the duodenum by combined barium-meal examination and oral cholangiography.

SUMMARY

1. A simple method for complete oral cholecysto-cholangiography is presented which requires minimal time and considerable reduction in patient exposure.

2. By the technic described, extrahepatic duct visualization was obtained in 85 per cent of 100 examinations.

Hospital for Joint Diseases
1919 Madison Ave.
New York 35, N. Y.

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SUMMARIO IN INTERLINGUA

Oral Cholangiographia Extrahepatic: Un Technica Simple e Fidel

Es describite un technica pro le "complete" cholecysto-cholangiographia oral, utilisante un synthetic cholagogo (Bilo-Vac) sin ulle drogas adjuvante. Le pellicula de signification es illo obtenite dece minutas post le repasto grasse, con le patiente in decubito dorsal, rotate per 15 grados verso le latere dextere. A iste momento le ductos es demonstrate le plus clarmente, e il ha approximativemente 30 a 40 pro cento de reduction in le dimensiones del vesica biliari. Le examine require un minimo de tempore, e le exposition del patiente es commensuratemente abbreviate.

Le ductos extrahepatic esseva visualisate per medio de iste technica in 85 pro cento de 100 examines.

Cobalt-60 Depth-Dose Corrections as Determined by Transmission-Dose Measurements

R. J. SCHULZ, M.Sc., G. A. COHEN, M. D.,[2] J. P. TSAI, M. D., and J. C. EVANS, M. D.

ALTHOUGH THE introduction of central-axis depth-dose data, measured in tissue-equivalent phantoms, elevated clinical radiation therapy to a semiquantitative discipline, it is generally recognized that in many instances these data, however accurate, fall short of indicating the true dose distribution in the patient because of tissue variations within the treatment field. This is especially true for orthovoltage x-ray therapy apparatus, where treatment through bone may result in differences as great as 50 per cent between the dose actually delivered and that indicated by depth-dose data (1). The problem of bone absorption is greatly reduced at cobalt-60 energies, but precise dosage of thoracic tumors remains as great a problem at such energies as it is for conventional x-rays. In order to determine the effect of tissues of different densities upon central-axis depth dose, a technic based upon transit-dose measurements and physically similar to schemes reported earlier (2–4) has been developed. In addition to providing factors which correct depth-dose data for tissue variations, a second requirement of this investigation was that the technic evolved should be simple enough to be carried out as a routine procedure by the resident staff.

Because the amount of radiation transmitted through a patient is a function of the thickness and density of tissues in the treatment field, transmission-dose measurements can be used to determine an effective absorption coefficient. If the transit dosimeter is collimated so that its readings are independent of field size, then these measurements result in what might be referred to as the effective linear absorption coefficient. When the experimentally determined effective absorption coefficient of a patient differs from that for material of unit density, the standard depth-dose data should be modified, in accordance with this difference, in formulating the treatment plan.

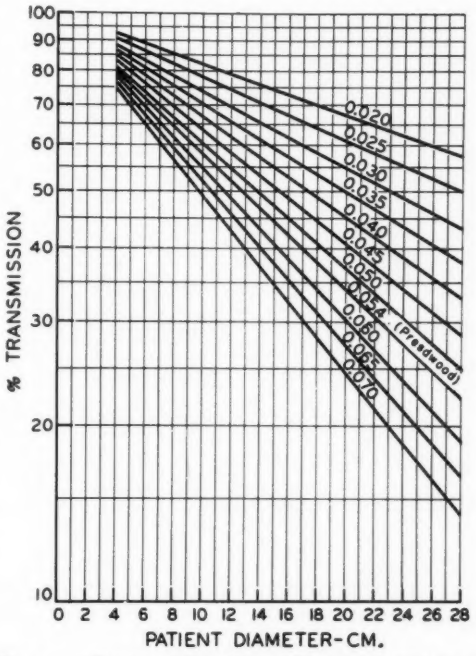


Fig. 1. Effective absorption coefficients plotted as a function of patient transmission and diameter.

The patient's effective absorption coefficient is determined by measuring, under identical conditions, the transmitted dose with and without the patient in place. These data, together with the patient's diameter, are used to solve the equation

$$D_t = D_o e^{-\mu' t} \qquad (1)$$

for μ', where D_t and D_o are the transit dosimeter readings with and without the patient in place and t is the patient's di-

[1] From the Department of Radiology, Albert Einstein College of Medicine, Yeshiva University and the Bronx Municipal Hospital Center, New York, N. Y. Accepted for publication in November 1960.

[2] American Cancer Society fellow, July 1, 1959, to June 30, 1960.

ameter. It is very important that the anteroposterior diameter be measured with the patient in his treatment position. In practice, in order to minimize calculations, μ' is determined graphically from a family of curves based upon this equation. These curves are shown in Figure 1.

In order to reduce the complexities of instrumentation, the standard 25-r Victoreen condenser ionization chamber is employed as the detector in the transit dosimeter. The remainder of the dosimeter consists of a simple clamp for supporting the ionization chamber and a straight-bore collimator made from cold-rolled steel. Both of these are mounted on the primary beam shield of the Keleket Rotaray Cobalt-60 unit, where accurate alignment of the dosimeter and the central axis of the treatment beam is easily achieved. The 25-r chamber was chosen because, for the range of treatment times normally employed and a fixed source-detector-distance of 110 cm., electrometer deflections range between one-quarter and three-quarters of full scale. A scale drawing of the dosimeter is shown in Figure 2.

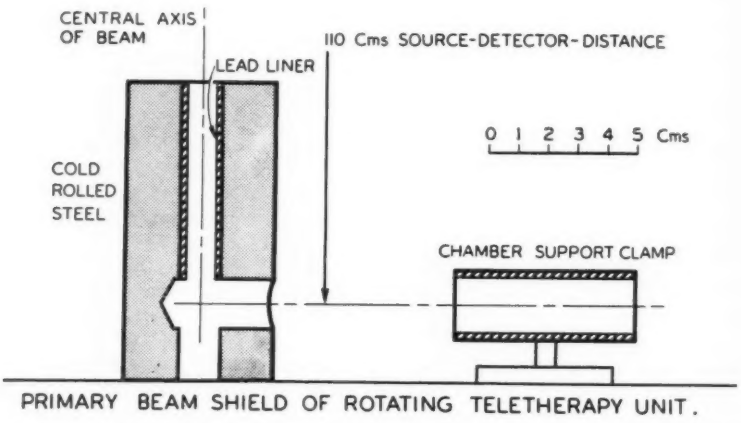

CENTRAL AXIS OF BEAM
110 Cms SOURCE-DETECTOR-DISTANCE
LEAD LINER
0 1 2 3 4 5 Cms
COLD ROLLED STEEL
CHAMBER SUPPORT CLAMP
PRIMARY BEAM SHIELD OF ROTATING TELETHERAPY UNIT.

Fig. 2. Scale drawing of straight-bore collimator mounted to primary beam shield of Keleket cobalt-60 unit.

The determination of the patient's effective absorption coefficient is the first step in arriving at a correction factor for central-axis depth-dose data. The second step involves its incorporation into a generalized equation for depth dose as per cent of surface dose. It has been assumed that an expression for central-axis depth dose can be written as

Per cent depth dose = 100 × (*inverse-square factor*) × (*scatter factor*) × (*absorption factor*) (2)

Inasmuch as the inverse-square-law factor is determined only by the geometry of the treatment set-up, *e.g.*, source-skin distance and lesion depth, it is constant for a particular situation and independent of variations in tissue density and source energy.

The scatter factor takes into account the radiation which is scattered to the central axis from the remainder of the irradiated volume. It is a function of the energy of the source, the field size, and the types of tissue in the irradiated volume. Because the contribution of scattered radiation to central-axis depth dose is relatively small for cobalt-60 gamma rays as compared with 200-kv x-rays, it has been assumed that a negligible error would be incurred by ignoring variations in the quantity of radiation scattered by tissues with densities differing from unity.

The absorption factor is an exponential term of the form $e^{-\mu d}$ where μ is a function of the energy of the source and, for Co-60 gamma rays, the density of tissue between the surface and the depth d. Experimentally determined values of μ',

TABLE I: CORRECTION FACTORS TO BE APPLIED TO CENTRAL AXIS DEPTH-DOSE DATA

Depth	Absorption Coefficient										
	.070	.065	.060	.054*	.050	.045	.040	.035	.030	.025	.020
0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
5	.92	.95	.97	1.00	1.02	1.05	1.08	1.10	1.13	1.16	1.19
10	.85	.90	.94	1.00	1.04	1.10	1.15	1.21	1.27	1.34	1.40
15	.79	.85	.91	1.00	1.06	1.14	1.24	1.34	1.43	1.55	1.67
20	.72	.80	.89	1.00	1.09	1.19	1.32	1.45	1.62	1.78	1.98

* Obtained with Presdwood under the experimental conditions described in the text.

the effective absorption coefficient, will be independent of the sequence of various tissues located along the central axis so that, for single field treatments, the exit dosimeter is not able to give information concerning dose for a specific depth. This is an important limitation on the application of transit dosimetry which will be discussed in greater detail below.

For the present, let it be assumed that the patient is homogeneous and therefore that μ', the effective absorption coefficient as determined by transit dosimetry, is equal to μ at any small segment of the patient's body. Inasmuch as the absorption factor is the only one of the three parts of equation (2) directly affected by a change in μ, density corrections will involve only this term. The correction factor may be expressed as the ratio of absorption in the tissue under consideration to the absorption in an equal thickness of unit density tissue:

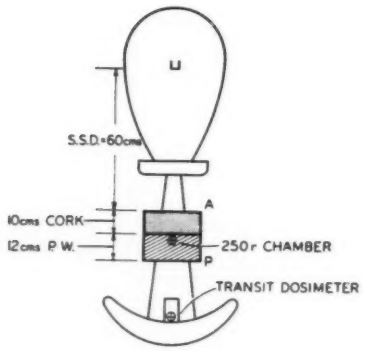
$$\frac{e^{-\mu' d}}{e^{-\mu_1 d}} = e^{d(\mu_1 - \mu')}$$

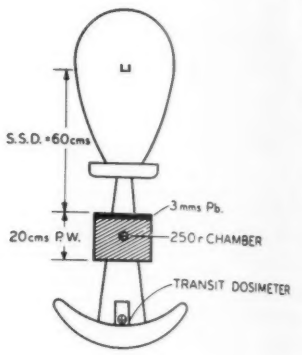
where μ_1 is the linear absorption coefficient for a unit-density tissue-equivalent material, μ' the experimentally determined effective absorption coefficient, and d the depth at which the dose is to be calculated. Table I gives values of this ratio for a range of absorption coefficients.

Therefore, by assuming the patient to be homogeneous, we have a method for correcting standard depth-dose data for variations in tissue density. A system of dosimetry that is based upon the assumption that the patient is homogeneous is, however, no great improvement upon one which assumes the patient to be of unit density. As mentioned above, the exit dosimeter gives information about the gross absorption properties of the patient but is unable to distinguish between a homogeneous absorber and one composed of tissues of widely differing densities. The correction factors listed in Table I, if determined by exit dosimetry and applied to a single portal treatment, can be used only in those cases where the tissue is homogeneous throughout the treatment field or where the tumor is centered between a symmetrical arrangement of nonuniform tissues.

If we now consider the case of a midline lesion treated through opposed portals—by far the most common treatment plan used in cobalt-60 teletherapy—we might expect that errors due to asymmetry would average out and that application of the factors in Table I to depth-dose data for both treatment fields would result in a calculated dose nearer to that actually delivered than indicated by depth-dose data alone. This notion was tested experimentally by assembling asymmetric phantoms composed as shown in Figure 3. Space was provided at midline level for a 250-r Victoreen ionization chamber. Each phantom was positioned at 60 cm. S.S.D. and exposed through a 10 × 10-cm. field anteroposteriorly and postero-anteriorly. In each case the calculated midline dose, when corrected in accordance with the transit-dosimeter reading, agreed within experimental error with the dose measured by the 250-r chamber.

In order to determine the range of midline depth-dose correction factors that may be encountered in clinical practice, a series of transit-dose measurements were made on terminal patients having no malignant involvement in the regions of the lung and





MIDLINE DEPTH DOSE (uncorrected)	A-P	P-A	TOTAL
Surface Dose	220r	220r	
% Depth Dose (11 cms)	48.3%	48.3%	
Depth Dose	106r	106r	212r
MIDLINE DEPTH DOSE (measured)	130r	109r	239r
MIDLINE DEPTH DOSE (corrected)			
Transit Dosimeter Reading with "Patient"	5.95	5.90	
Transit Dosmeter Reading without "Patient"	14.8	14.8	
Percent Transmission	40.2	39.8	
Effective Absorption Coefficient (fig.1)	0.042	0.042	
Correction Factor (Table I)	1.13	1.13	
Corrected Depth Dose =	(212r x 1.13) =		240r

MIDLINE DEPTH DOSE (uncorrected)	A-P	P-A	TOTAL
Surface Dose	315r	315r	
% Depth Dose (10cms)	52.2%	52.2%	
Depth Dose	164r	164r	328r
MIDLINE DEPTH DOSE (measured)	136r	166r	302r
MIDLINE DEPTH DOSE (corrected)			
Transit Dosimeter Reading with "Patient"	6.0	6.0	
Transit Dosimeter Reading without "Patient"	21.1	21.1	
Percent Transmission	28.4%	28.4%	
Effective Absorption Coefficient, (fig.1)	0.063	0.063	
Correction Factor (Table I)	0.92	0.92	
Corrected Depth Dose	(328r x .92) =		302r

Fig. 3. Experimental verification of transit dosimetry applied to opposed ports.

TABLE II: RESULTS OF TRANSIT DOSIMETRY APPLIED TO NORMAL LUNG AND MEDIASTINUM

Patient	Diameter (cm.)	Lung		Mediastinum	
		μ'	Midline Correction Factor	μ'	Midline Correction Factor
S.C.	21	0.023	1.32	0.049	0.96
J.N.	17			0.056	0.98
D.W.	20	0.033	1.24		
J.H.	26	0.040	1.21		
J.M.	18	0.031	1.24	0.067	0.89
J.G.	22	0.026	1.34	0.065	0.89
W.B.	21	0.027	1.32	0.061	0.93
M.M.	25	0.029	1.28	0.048	0.97
J.B.	22	0.030	1.30	0.062	0.93
C.M.	18	0.022	1.34	0.064	0.95
J.C.	20	0.040	1.15	0.068	0.88
A.P.	24			0.069	0.85
AVERAGES		0.030	1.28	0.061	0.92

TABLE III: TRANSIT DOSIMETRY APPLIED TO PATIENTS WITH LUNG TUMORS

Patient	A-P Diameter (cm.)	Field Size	Per cent Transmission	μ'	Midline Correction Factor
S.C.	25	10 × 17	26	0.054	1.00
B.M.	22	10 × 15	41	0.040	1.17
J.M.	20	12 × 20	41	0.045	1.10
J.H.	26	14 × 17	32	0.044	1.15
J.N.	17	13 × 14	42	0.050	1.03
T.U.	18	8 × 10	45	0.044	1.11

mediastinum. In this series the exposure dose was limited to 150 r through a 4 × 4-cm. field. Average values of the effective linear absorption coefficients for pulmonary and mediastinal fields are 0.030 and 0.061 respectively. From these data, shown in Table II, one should expect midline depth-dose correction factors to range between 0.92 and 1.28 for treatment fields centered over the lungs. Table III gives detailed transit-dose data for a group of patients having primary or metastatic lung tumors. Because of the size and near unit density of the tumors, midline depth dose correction factors ranged between 1.00 and 1.17.

It was thought that, by using the range of experimentally determined absorption coefficients for normal lung and mediastinum, relatively accurate estimates of the effective absorption coefficients of patients receiving radiotherapy to these regions could be made from diagnostic films. A blind study was undertaken by one of the authors (G.A.C.) to estimate the effective absorption coefficient at the center of the treatment field and then to compare

his estimates with the results obtained by transit dosimetry. The appearance, *i.e.*, density, of the area covered by the treatment field, was subjectively compared to the mediastinum and uninvolved lung. Upper and lower limits of the effective absorption coefficient for normal mediastinum and lung were taken at 0.061 and 0.030 respectively. It was found that midline depth-dose correction factors calculated from these estimated absorption coefficients differed as much from the experimentally determined factors as the experimentally determined factors differed from unity. In short, as much error was introduced by the estimated correction factors as would be incurred by using standard depth-dose data alone.

DISCUSSION

Because the method described for correcting central-axis depth-dose data for variations in tissue density has proved accurate by phantom measurements and may be carried out on a routine basis by the resident staff, correction factors are being determined for all thoracic treatment fields. As can be seen from the data in Table III, there is no single correction factor which can be applied to thoracic fields. Each patient, if any corrections are to be made, should be evaluated separately.

It has been noted that the appearance of the chest roentgenogram cannot be used as a guide for making quantitative estimates of the patient's effective absorption coefficient.

An obvious extension of this method would be to rotational therapy which is, in essence, a series of opposed ports. This has not been done as yet but is contemplated.

SUMMARY

A method for correcting the central-axis depth dose for tissue density variations is described. The only equipment needed is a Victoreen condenser r-meter and an inexpensive collimator of simple construction. The technic, which is based upon patient transmission, involves three measurements: (*a*) a transit dosimeter reading of radiation transmitted by the patient during the course of a routine treatment, (*b*) a transit dosimeter reading made under identical conditions but with the patient removed, and (*c*) the patient's anteroposterior diameter. With the aid of data presented above, which should be applicable to all cobalt teletherapy apparatus, the appropriate correction factors are readily obtained.

Albert Einstein College of Medicine
1300 Morris Park Avenue
Bronx, N. Y.

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(*Pro le summario in interlingua, vider le pagina 817*)

Some Aspects of the Microcirculation of a Transplantable Experimental Tumor[1]

MORTON M. KLIGERMAN, M.D., and DORA K. HENEL, B.A.

ATTEMPTS TO increase the oxygen tension of experimental tumors by means of vasodilators (1) focused our attention on the microcirculation of a transplantable tumor, hepatoma 134, in C3H/CRGL mice. Using the Algire chamber technic (2), we have sought (Fig. 1) to determine whether the response to pharmacologic agents of vessels supplying the tumor is similar to the response of somatic vessels. A diagrammatic cross section of the chamber placed in the skin of the back of the mouse is illustrated (Fig. 2). Observations on the anatomic development of the vascular supply to this tumor in our laboratory support the early work of Algire and his associates (3, 4) to a considerable degree, although not entirely. The pharmacologic tests were done on unanesthetized animals.

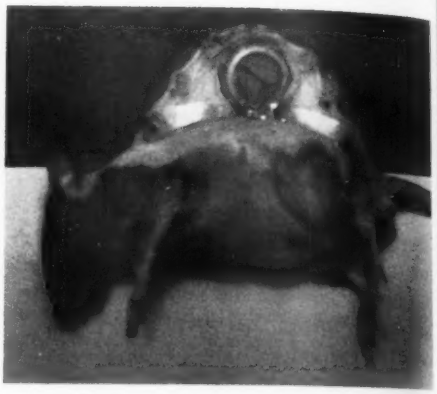


Fig. 1. Algire chamber, access type.

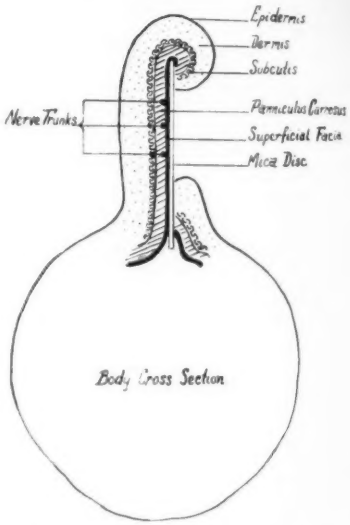


Fig. 2. Cross section through Algire chamber, diagrammatic representation.

ANATOMIC DEVELOPMENTS

Tumor fragments ranging in size from 600 to 1,000 microns in diameter are placed next to one of the cutaneous nerves of the skin located between the panniculus carnosus and the superficial fascia. On the day of transplantation these fragments appear opaque. From two to fifteen days later, usually by the third to fifth day, the first vascular invasion is observed. The vessels are capillary structures whose diameters vary so that portions appear as sinusoids. Most important is the fact that these capillaries are supplied and drained by venules arising from existing somatic veins (Fig. 3). One to three days after this venous circulation is established, the first evidence of arteriolar supply to the capillary bed is seen (Figs. 4, 12, 13). At this time the portion of the tumor invaded by vessels clarifies, becoming relatively translucent (Fig. 5). It is of interest that within twenty-four hours punctate hemorrhages developed in 25 per cent of our specimens (Fig. 11). Not until the arteriolar supply is established does growth of the tumor occur. This arteriolar supply originates from existing somatic vessels. Because

[1] From the Department of Radiology, School of Medicine, Yale University, New Haven, Conn. Work supported by U. S. Public Health Service Grant, Numbers C-4391, C-4391-C1, and C-4391-C2. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4–9, 1960.

of the proximity of the tumor transplant to the cutaneous nerve trunk, the venous and arterial connections with the capillary bed usually come from the respective vessels of the nerve, although other arteries and veins of the skin have been seen supplying the tumor. The capillary

Fig. 3. Venous capillary bed five days after transplantation. Large black vessel through center of photograph is major vein of cutaneous nerve. Single arrows on capillary bed. Double arrows on venules. Mouse #4125. Original magnification × 32

bed is characterized by shunts which bypass large sections of the capillary network. These shunts appear no different in structure from the vessels in the networks themselves and are endothelial in nature.

ACTION OF ACETYLCHOLINE, EPINEPHRINE, AND CARBON DIOXIDE

The effects of acetylcholine and epinephrine on the arterioles and normal arteries supplying the tumor were compared with their effects on small somatic vessels. With a cinephotomicrographic technic, obtaining sharp definition of the vessels was a problem. This was due mainly to the presence of tumor cells and host cells overlying the vessels and combining to form myriads of refractile bodies. To some extent the overall thickness of the specimen (800–1,000 microns) is a contributing factor. The gross changes in the arterioles and the capillary flow, however, can be observed. A zirconium

Fig. 4. First arteriolar supply seven days after transplantation. Single arrow is artery to the nerve Double arrow is arteriole to the tumor capillary bed. Mouse #4125. Original magnification × 32

light source was used and the film (Anscochrome, 3,400 Kelvin) was run at approximately 32 frames per second.

Acetylcholine: The consistent response to acetylcholine of arterioles to the tumor and of small somatic arteries unrelated to the tumor is constriction. This occurs from two to five minutes after the intraperitoneal injection of 0.1 to 0.6 mg. of the drug and is considered the late effect (Figs. 6, 8, 9, 13, 15, and 16). The onset of this contraction may be slightly earlier in the tumor arterioles than in the small somatic arteries situated at some distance, which are of larger caliber. The time of contraction of an arteriole to the tumor, however, is synchronized with the contraction of the small somatic artery from which it branches. This mother artery is usually smaller in caliber than the somatic arteries at a distance from the tumor and probably represents a more terminal division artery or somatic arteriole. Once contraction begins, it progresses so that some tumor arterioles and somatic arteries completely disappear (Fig. 9). The degree of the contraction described varies directly with the dose of the drug. From seven to eighteen minutes after administration of acetylcholine, these vessels slowly begin to dilate and return to the steady state (Fig. 10).

During the period when contraction of the tumor arterioles and small somatic

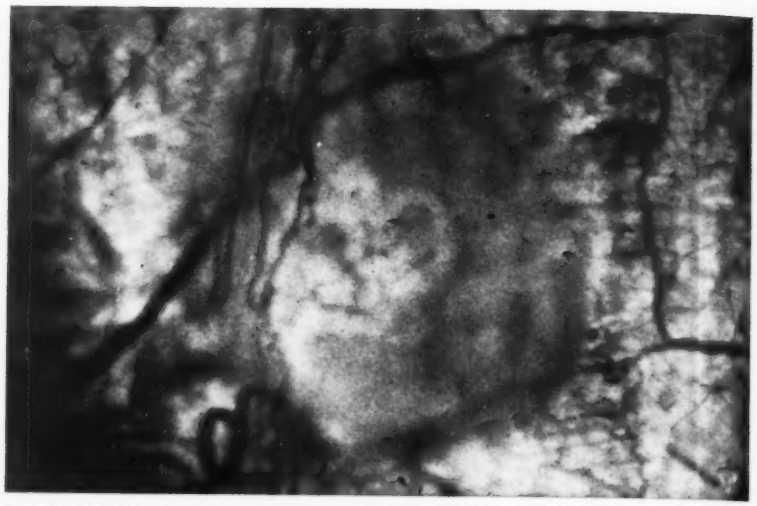
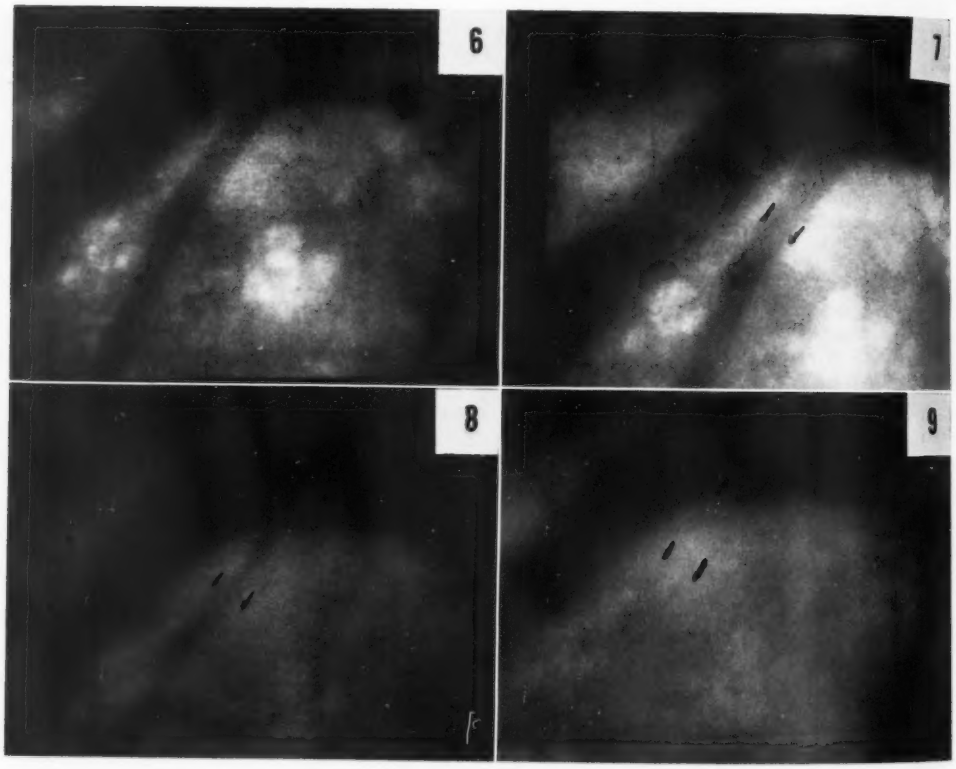


Fig. 5. Clarification of portion of transplant invaded by blood vessels nine days after transplantation. Mouse #885. Original magnification × 12.5



Figs. 6–9. Mouse #793.

Fig. 6. Steady state, small somatic artery and somatic vein (larger vessel). Original magnification × 55.

Fig. 7. Effects of acetylcholine thirty seconds after drug; dilatation of small somatic artery. This effect, when it occurs, is transient. Original magnification × 55

Fig. 8. Effect of acetylcholine four minutes after drug, showing beginning contraction of the small somatic artery. This is the "epinephrine effect," due to discharge of the adrenal medulla. Original magnification × 55

Fig. 9. Effect of acetylcholine six minutes after drug, showing complete contraction of small somatic artery. Original magnification × 55

arteries is marked but not yet complete, the constriction is segmental, producing an oscillating knobby appearance.

Less consistent is the early response to acetylcholine. Not infrequently there is a very rapid, transient constriction within fifteen seconds after injection, lasting about thirty seconds. This is followed by equally rapid return to normal caliber. This early effect might be due to the shock of intraperitoneal injection. It is not observed, however, when normal saline of the same volume is injected. Occasionally there is transient dilatation of the tumor arteriole or somatic arteries (Figs. 7 and 14) either immediately after injection or, more commonly, after the major contraction but before a return to the steady state.

Blood flow rate through the arterioles of the tumor and small somatic arteries controls the rate of flow in the respective capillary beds. When constriction is just beginning, flow through the tumor arterioles and somatic arteries is increased. As constriction becomes greater, circulation slows and may stop completely. The speed of flow through the capillary bed is usually in the same direction as that through the afferent vessels. When complete contraction of the arteriole takes place, however, circulation within the capillary bed is related to the venous circulation (see below). Although the rate of flow is for the most part related to the caliber of the afferent vessels, slowing may occur one and a half to three minutes after injection of acetylcholine, with or without minimal constriction of the tumor arterioles and small somatic arteries. This might well be related to changes in cardiac output, which has not been correlated with these observations.

Change in the direction of flow is observed in somatic arteries, capillary bed and venules of the tumor, and various somatic veins. Terminal arterioles to the tumor have not shown reversal of flow. The small arteries of the skin of the mouse form a network similar to but not as extensive as that of the veins. Reversal of

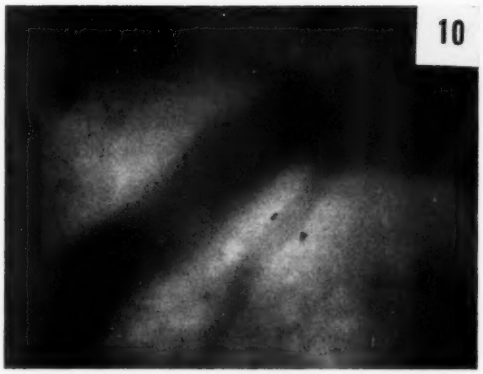


Fig. 10. Mouse #793. Seven minutes after acetylcholine the small somatic artery has dilated and is returning to a steady state. Original magnification × 55

flow in some somatic arteries does occur following contraction. In venules and veins the flow may be reversed as early as four seconds after injection. The basis for all these changes in direction is altered pressure in the vascular supply of the skin; they are indicative of the anastomotic character of arteries as well as veins, providing alternate avenues of flow.

Carbon Dioxide: Observations on the vessels in the Algire chamber when a mixture of carbon dioxide 6 per cent and oxygen 94 per cent is tested show several different reactions. This is believed to be due to variation in the degree of reflex pressor action. There may be immediate and marked decrease in capillary flow, complete cessation of flow, and at times reversal of flow through the capillary bed. Also, transient dilatation of the arterioles is observed in some animals within four to ten seconds after inhalation of carbon dioxide.

Carbon Dioxide and Acetylcholine: The response of the tumor arterioles and small somatic arteries to acetylcholine of the same dosage as above, while the animal inhales a mixture of carbon dioxide 6 per cent and oxygen 94 per cent is consistently an increased flow through the capillaries within thirty seconds after injection. The effect is transient, with the usual contraction of the afferent vessels beginning one and a half to two minutes

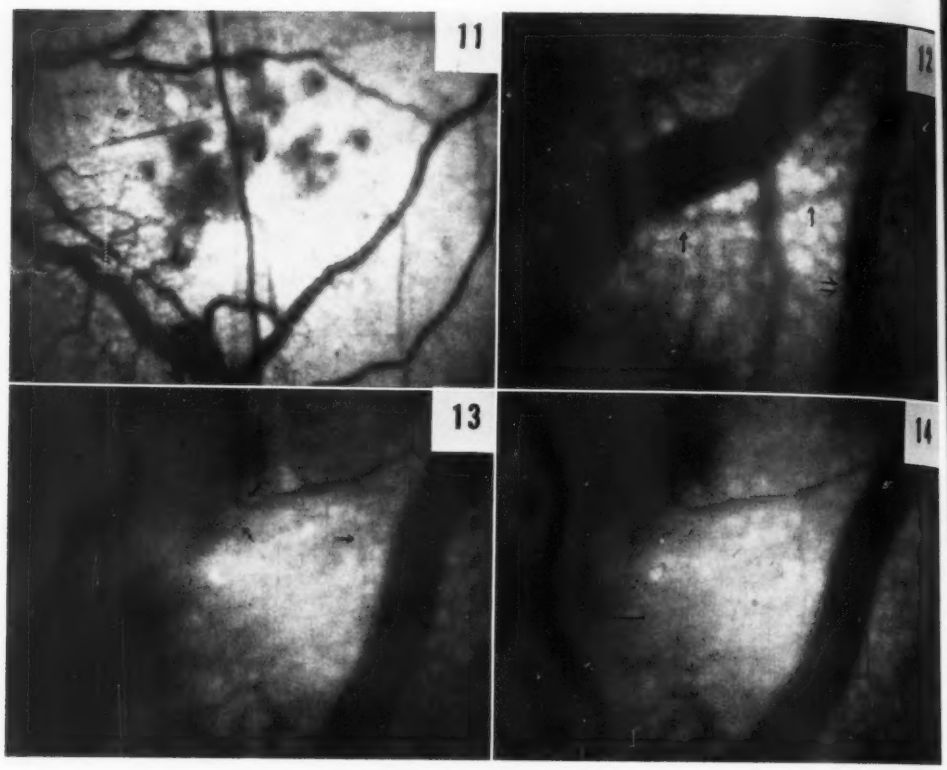


Fig. 11–14. Mouse #552.

Fig. 11. Punctate hemorrhages in tumor transplant at five days, twenty-four hours after first visualization of arteriole to tumor. Original magnification × 12.5

Fig. 12. First arteriole (single arrows) to tumor showing its origin from an existing somatic artery (double arrows) five days after transplantation. See Fig. 13 for continuation into tumor. Original magnification × 55

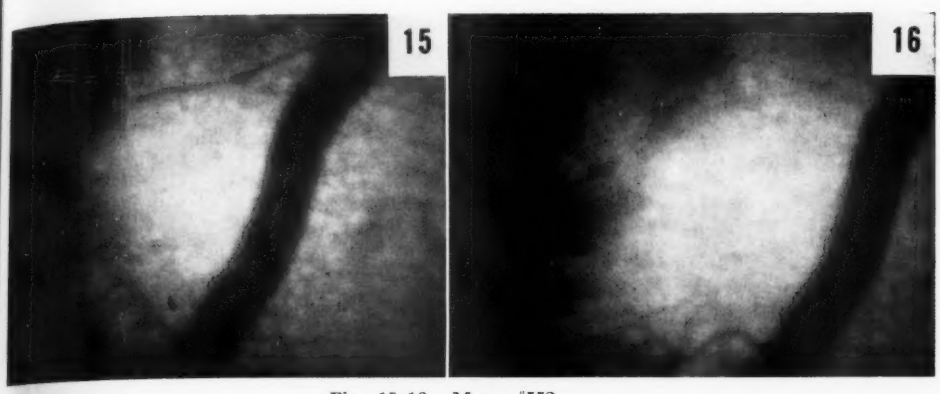
Fig. 13. First arteriole to the tumor five days after transplantation, traversing tumor mass. Note three capillaries (arrows). Original magnification × 55

Fig. 14. Effects of inhaling carbon dioxide 6 per cent and oxygen 94 per cent. Slight dilatation of the arteriole to the tumor ten seconds after start of gas mixture. Original magnification × 55

later. Return to the steady state is similar to that of animals treated by acetylcholine alone.

Epinephrine: The response of small arterioles to the tumor and of small somatic arteries to epinephrine, 0.004 mg. intraperitoneally, is consistent, and the effect is independent of the time that the epinephrine is added to the system in relation to carbon dioxide inhalation or acetylcholine injection. As expected, the afferent vessels contract within thirty seconds. As constriction proceeds, there might be reversal of flow in the veins of the skin and slowing of the capillary flow which would come to a standstill when marked narrowing of the tumor arterioles or small arteries takes place. Reversal of flow in somatic arteries with collateral circulation can be seen. Relaxation of the tumor arterioles and somatic arteries begins six to ten minutes after injection and the steady state is achieved in seven to twenty-seven minutes. In short, the response of the vessels to epinephrine is similar to the late effect of acetylcholine.

The response of the blood supply of the tumor transplant to all the drugs tested mimicked the response of somatic vessels located at some distance from the tumor itself. Flow through the capillaries, as expected. is under direct control of the



Figs. 15–16. Mouse #552.

Fig. 15. Effects of acetylcholine on tumor arteriole ten minutes after administration of drug. Beginning contraction is seen. Original magnification × 55

Fig. 16. Effects of acetylcholine on tumor arteriole sixteen minutes after drug. Severe constriction of arteriole due to "epinephrine effect." Capillaries blanched. Original magnification × 55

arteriolar supply. A decreased flow rate through the arteriole or constriction of the arteriole causes a decreased flow through the capillary bed.

DISCUSSION

The initial capillary bed, supplied purely by venous blood in this transplanted tumor, is of interest in view of the similar observations made by Humes and Akers (6) on the vascular response to infestation by Trichinella larvae. They found the initial vascular reaction around the invaded muscle fiber to be a network of venous capillaries. Although hepatoma 134 originated as an induced tumor (7), it has demonstrated 98 per cent takes in successive transfers in our laboratory and elsewhere. Despite this, some host resistance is present. Fragments less than 500 microns are grown in the chamber with difficulty, and host cells soon cover the specimen. The question is raised as to whether this type of initial venous blood supply is comparable in its development to that in a tumor arising spontaneously in a particular host. In the carcinomatous transformation of a particular cell, the blood supply to the cell would necessarily have to be from capillaries with an arteriolar supply. One would theorize that, as this cell reproduces, the normal arteriole-capillary-venule vascular supply would grow with it. Differences in the curability of spontaneous as compared with transplanted tumors, as demonstrated by Scholler and co-workers (8, 9), may be due in part to the variation in the vascular structure, in addition to any degree of immune response in isologous transplants.

At no time was the differentiation of tumor capillaries into arterioles or venules observed as reported by Algire (4). The earliest capillaries could always be traced to an adjoining pre-existing somatic vein. Arteriolar supply could always be traced to a pre-existing somatic artery. Because the deep portion of these tumors could not be examined for vascularity, the question is raised as to whether the initial capillary invasion of the tumor could not in some instances develop from the arteriolar side of the circulation. I believe it reasonable to assume that the processes consistently and uniformly seen on the surfaces and margins of the tumor were repeated at its depth. It is of interest, furthermore, that punctate hemorrhages in the tumor occur only after the arteriolar supply is established and can be seen on the surface and periphery of the growth. It is my feeling that, if capillaries initially supplied by arterioles at the depth of the tumor were present, hemorrhages could be noted there in some instances when arteriolar supply cannot be seen on the surface.

It is proposed that the hemorrhages are due to the increased intracapillary pressure which occurs with the initiation of arteriolar supply. Capillaries of a transplanted mammary adenocarcinoma were shown by Algire *et al.* (10) to be more fragile than those in the surrounding normal structures. They found a greater degree of damage from the injection of bacterial polysaccharide in the tumor capillary bed.

The segmental contraction of tumor arterioles and small arteries, with an oscillating knobby appearance, seen after administration of the various agents tested is similar to that reported by Arendt *et al.* (5) on application of moccasin venom to the arterioles of the hamster's cheek pouch.

The observation that a small somatic artery and an arteriole supplying the transplanted tumor respond to three pharmacologic agents in the same direction is to be expected in view of the evidence that the blood supply to the tumor arises from existing somatic vessels. This is contrary to the observation of Bierman *et al.* (11), who believe that vessels within some neoplasms would not react to vascular constrictor agents as do normal vessels. The similarity of the late acetylcholine effect to that of epinephrine alone is demonstrated. The reason is that acetylcholine, especially in large doses, leads to discharge of the adrenal medulla, resulting in the release of epinephrine. A similar late effect, to a lesser degree, was observed with 0.1 mg. of acetylcholine. In selecting drugs and dosages for prolonged dilatation of vessels, late constricting action must be avoided.

Attempts will be made to build the Algire chamber around spontaneously occurring mammary adenocarcinoma in the C3H mouse to determine the origin of the vascular supply and its response to various pharmacologic agents.

SUMMARY

In mice with a transplantable carcinoma, it was demonstrated that the arterioles supplying the tumor arise from somatic vessels after an initial venous capillary bed is formed. The response of these arterioles to three pharmacologic agents—acetylcholine, epinephrine, and a mixture of 94 per cent oxygen and 6 per cent carbon dioxide—are similar to those of somatic vessels distant from the tumor. Some of the vessels making up the capillary bed may be sinusoids, but in all instances the flow through these endothelial vessels is subject to the control of the arteriolar supply.

ACKNOWLEDGMENTS: I wish to acknowledge the opportunity to have initiated this work in the Department of Radiology, Stanford University, and to express my gratitude to Dr. Henry S. Kaplan and Dr. Robert F. Kallman for the help they provided at that time. I also want to thank Dr. George Fulton, Department of Biology, Boston University, for his invaluable advice. Mrs. Becky Glezen provided valuable technical assistance.

789 Howard Avenue
New Haven 4, Conn.

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SUMMARIO IN INTERLINGUA

Certe Aspectos del Microcirculation de un Transplantabile Tumor Experimental

In muses portatores de transplantas carcinomatose, il esseva demonstrate que le arteriolas que alimenta le tumor ha lor origine in vasos somatic post que un vasculatura veno-capillari initial es formate. Le responsas de iste arteriolas a tres agentes pharmacologic—acetylcholina, epinephrina, e un mixtura de 94 pro cento de oxygeno e 6 pro cento de bioxydo de carbon—es simile al responsas de vasos somatic distante ab le tumor. Certes del vasos que constitue le vasculatura capillari pote esser sinusoides, sed in omne casos le fluxo a transverso iste vasos endothelial es subjecte al controlo del alimentation arteriolar.

SUMMARIO IN INTERLINGUA

Correction de Doses in Profundor ab Cobalt-60, Determinate per Mesurationes de Doses de Transmission

(*pagina 805*)

Ben que le factor del absorption in osso es grandemente reducite in le therapia a cobalt-60 in comparation con irradiation a orthovoltage, le problema del precise dosage a tumores thoracic remane. Le autores ha elaborate un methodo pro le correction del dose in profundor al axe central pro le densitate del tissu in le caso individual. Le sol apparatura requirite es un r-metro condensatori Victoreen e un incostose collimator de simple construction. Le technica, basate super le transmission per le patiente, require tres mesurationes: (1) Un lectura dosimetric de transito del radiation transmittite per le patiente durante un tractamento routinari; (2) un lectura dosimetric de transito effectuate sub precisemente le mesme conditiones sed con le patiente absente; e (3) le diametro anteroposterior del patiente. Es presentate datos que permitte prestemente le obtention del appropriate factores de correction. Istos es sin dubita applicabile a omne apparaturas de therapia a cobalt.

Disease Conditions in Animals, with Radiographic Findings, That Are Also Present in Man[1]

STUART A. PATTERSON, M.D.

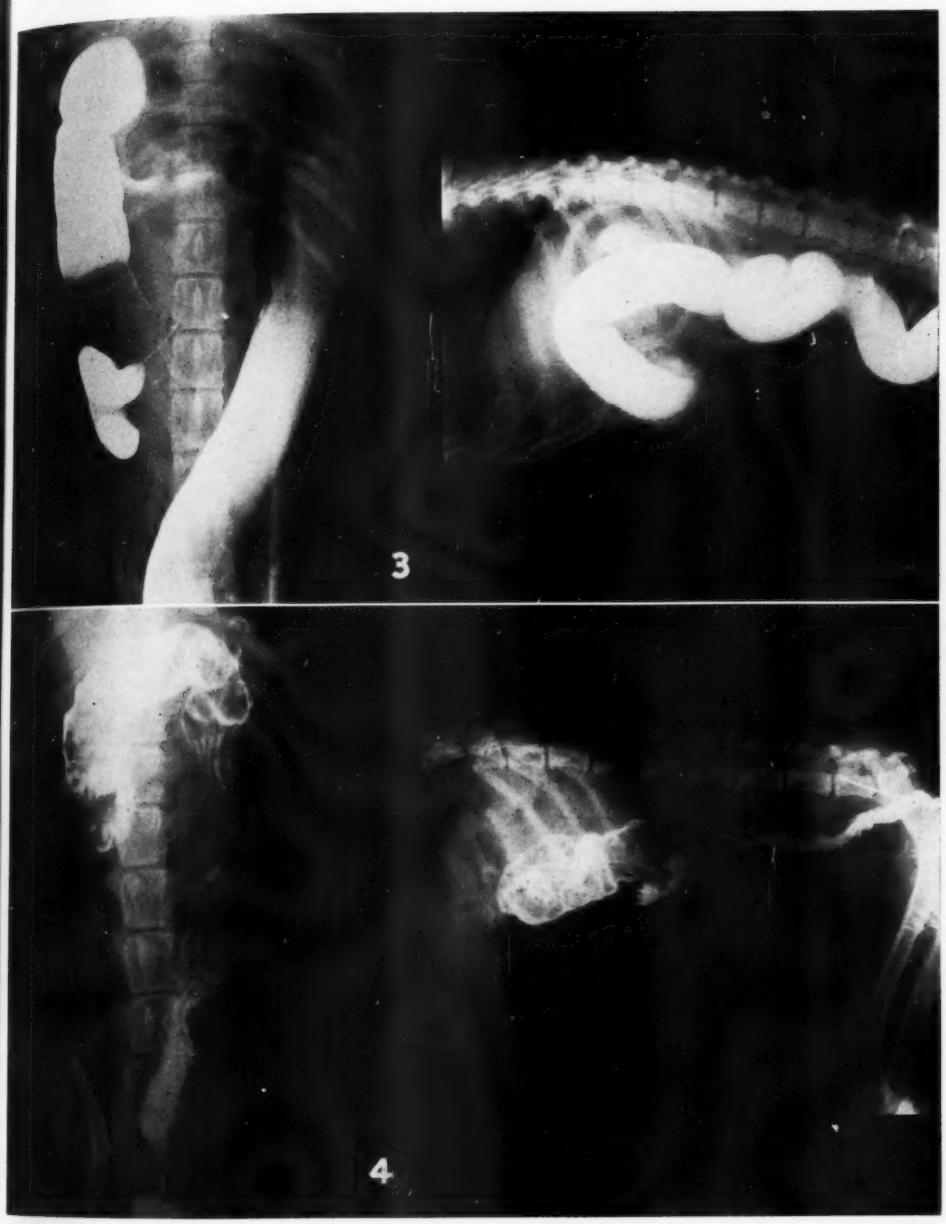
THE PURPOSE of this paper is to present and discuss briefly some examples of diseases which occur in both animals and man and to point out that many of these conditions are so nearly identical in the two groups that it is difficult to distinguish them as to either etiology or pathology. A complete review of the subject is not intended.

Fig. 1. Intestinal obstruction in a dog, associated with intussusception. Decubitus studies show gas-capped fluid levels typical of obstruction.

Fig. 2. Impaction of bone chips in the distal portion of the ileum of a dog. The distention of the small intestine proximal to the obstruction and the gas-capped fluid levels are clearly visualized.

Although animals have been extensively used experimentally, the employment of animal patient material has not been fully exploited. Much has been done to create pathologic conditions in animals for purposes of study. The cases presented in this paper are examples of spontaneous disease in actual animal patients. As

[1] From the Department of Radiology, School of Veterinary Medicine, Colorado State University, Fort Collins, Colo., and the Department of Radiology and School of Medicine, University of Colorado, Denver, Colo. Presented at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15–20, 1959. Received for publication in 1961.



Figs. 3 and 4. Intussusception in a dog. Barium-enema examination (Fig. 3) shows a defect in the region of the ascending colon, as a result of intussusception. The cecum is a free pouch. Following evacuation there is an increase in the amount of intussusception (Fig. 4).

such they afford a unique and significant opportunity for clinical investigation inasmuch as many of them are virtually duplicated in man.

It is difficult, and frequently impossible, to state the exact percentage of the animal population inflicted with any one of these various conditions. In many instances the

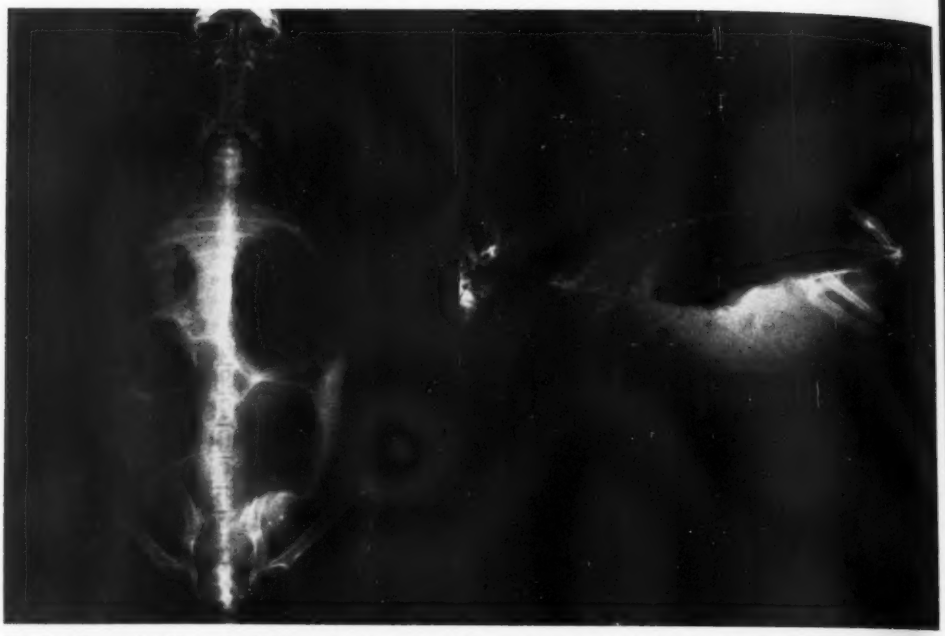


Fig. 5. Example of intestinal obstruction due to fecal impaction in a chinchilla, showing marked gaseous distention of the intestinal tract, with fluid levels.

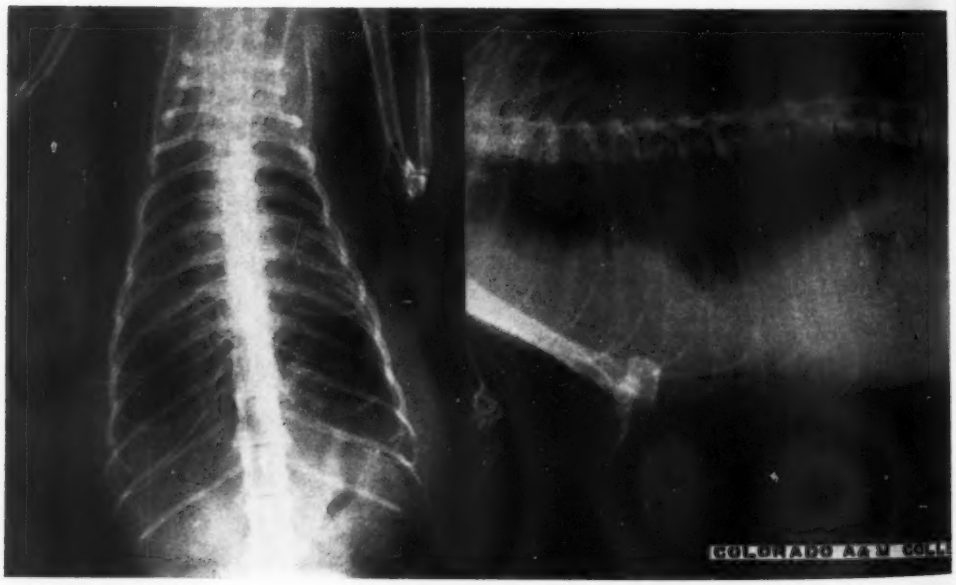


Fig. 6. Pneumonia with empyema in a cat. The most striking finding in this instance is the fluid in the pleural cavity. The hazy density identified in the lung field of the postero-anterior study is probably at least partially due to the pneumonitis.

figures have not been compiled, due, at least in part, to the fact that the science of radiology is actually in its infancy in veterinary medicine.

Figure 1 illustrates a case of intestinal obstruction in a dog. The distention of the bowel and the air-fluid levels are distinctly seen. The cause of the obstruction was intussusception at the ileocecal junction. This was relieved surgically, with relative ease, with a successful outcome.

The most common cause of intestinal obstruction in the dog is the ingestion of foreign bodies, with intussusception probably next in order. Small-bowel obstructions are rare in horses, cattle, and sheep, but large-bowel obstruction due to fecal impaction is of quite frequent occurrence in larger animals. Figure 2 shows a small-bowel obstruction in the distal ileum of a dog, associated with impaction of bone chips.

Fig. 7. Perforated hollow viscus in a dog; free air under the diaphragm in the left lateral decubitus position.

Fig. 8. Perforated hollow viscus in a dog due to an ulcer in the distal ileum. The view to the right shows the entire abdomen. Free gas is demonstrated in the prone position with a lateral horizontal beam. The left lateral decubitus view is also shown.

As noted above, intussusception is relatively common in the dog. A barium-enema examination in such a situation shows the usual invagination of the ileum into the ascending colon. The cecum is a small separate blind pouch. At

Fig. 9. Actinomycosis (lumpy jaw) in a cow. Note the swelling of the left side of the face and jaw. This is a rather typical appearance.

We have not tried to reduce these intussusceptions by barium enema, but the procedure has been done in other institutions and is approximately as successful in dogs as in man.

Intussusception in dogs is about as common as in man but, as suggested above, is rarely seen in other animals. We have never observed it in a cat, although it has been reported in that animal. It occurs rarely in cattle and with extreme infrequency in horses. Small-bowel obstructions do, however, take place in other animals. Figure 5 illustrates a case in a chinchilla, due to food impaction. While in dogs and cats intestinal surgery is feasible, in the chinchilla it is impossible because the intestine is of the

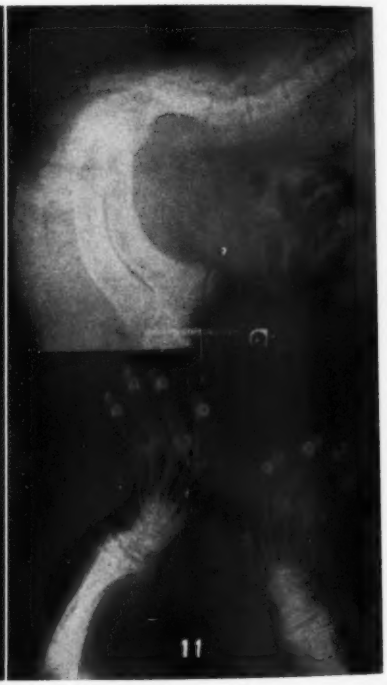


Fig. 10. Extensive osteogenesis imperfecta in a Siamese cat.
Fig. 11. Osteogenesis imperfecta in an Indian tiger, with extensive deformity. The animal sustained fractures from minimal trauma, including a jump from a low elevation, in which it landed on its feet.

the time of examination (Fig. 3) the intussusception was partially reduced by the barium enema. It recurred (Fig. 4) after evacuation, with involvement of the splenic flexure of the colon.

consistency of wet cigarette paper If operation is resorted to, the bowel is not entered but is manipulated from the outside after the peritoneal cavity has been opened. In the case shown here

death occurred shortly after the examination.

Pneumonia in cats is of virus origin but is often complicated by empyema due most commonly to a secondary bacterial infection. In the case shown in Figure 6 there was considerable empyema, which cleared with the pneumonitis, leaving no residue. Surgical drainage was not attempted, though it is sometimes done. Antibiotics were given. Pneumonia in cats may be of serious import, and treatment should be instituted promptly to prevent a fatal outcome. Pneumonitis occurs also in dogs, but much less frequently.

In man a perforated peptic ulcer is quite common, resulting in free air in the peritoneal cavity. In dogs and cats, and most other animals, perforated peptic ulcers are virtually unknown (no worries!). The free air in the peritoneal cavity of the dog seen in Figures 7 and 8 was due to a non-specific and very unusual ulceration in the distal ileum. Penetrating ulcers are fairly common in calves, usually occurring in the fourth or true stomach.

Fig. 12. Osteogenic sarcoma in the foreleg of a dog. Extensive destruction of the distal end of the radius with new bone proliferation is shown. This is the most common appearance of osteogenic sarcoma in the dog.

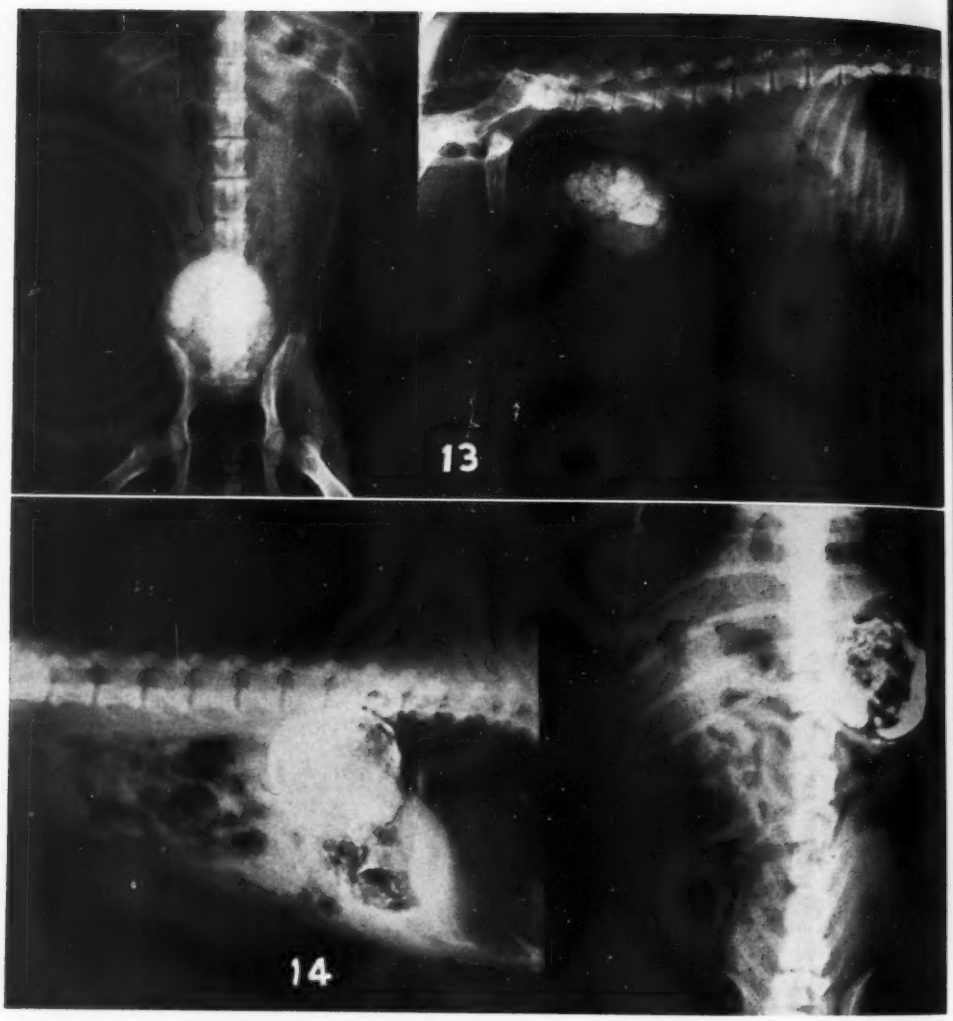


Fig. 13. Almost complete filling of the urinary bladder by cystic calculi, in a dog.
Fig. 14. A sponge-rubber ball in the fundus of the stomach of a dog. This became swollen after entry into the stomach.

Diaphragmatic hernias are seen rather frequently in dogs and rarely in cats. They are usually post-traumatic in origin and almost never involve the esophageal hiatus. Often a large part of the abdominal content is displaced into the thoracic cavity and can be replaced surgically. Diaphragmatic hernia is fairly common in cattle, particularly in young calves, where it is probably primarily congenital in origin.

A disease known for many years to occur in animals and man is actinomycosis. Figure 9 shows actinomycosis of a cow (lumpy jaw). Changes in the bony structures of the maxilla are sometimes seen. The active organism, *Actinomyces bovis*, is found in cattle, man, and some other species. It has been described in wild elk. The mandible is the usual site of infection in cattle, though the maxilla may be involved. When the bone is infected, it becomes enlarged and honeycombed as the result of destructive rare-

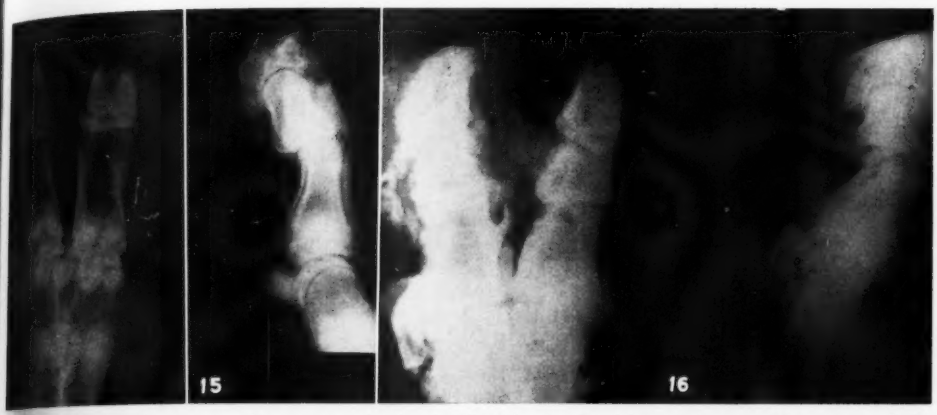


Fig. 15. Foot rot in a cow. Changes are clearly visualized in the distal interphalangeal joint of one of the claws.
Fig. 16. Extensive changes in the foot of a cow indicating long-standing foot rot.

Fig. 17. Marked distention of the esophagus in a Chihuahua dog, due to cardiospasm.

faction and regenerative proliferation. Another organism, *Actinobacillus lignieresi*, produces soft-tissue changes primarily.

Osteogenesis imperfecta is relatively rare in man and is actually poorly understood. It occurs in almost all species of cats, being more common in the Siamese cat (Fig. 10) than in other species, although it has been described in wild bobcats and in the Indian tiger (Fig. 11). We do not recognize this condition in dogs and larger animals.

Osteogenic sarcoma is not uncommon in dogs, its usual location being at the distal end of the foreleg or in the relatively similar area in the hind leg (Fig. 12). The tumor is rare in horses and cattle and, if seen, usually involves the jaw.

Cystic calculi are found fairly frequently in the urinary bladder of dogs (Fig. 13) and occur in horses and in cattle. They are rare in cats. Urethral calculi constitute a common and important disease in cattle.

Foreign bodies are relatively common in animals. Figure 14 shows a sponge-rubber ball swallowed by a dog. In the stomach the gastric juices caused it to swell to a size that would have made its ingestion impossible. Almost everything that is small enough to pass through the thoracic

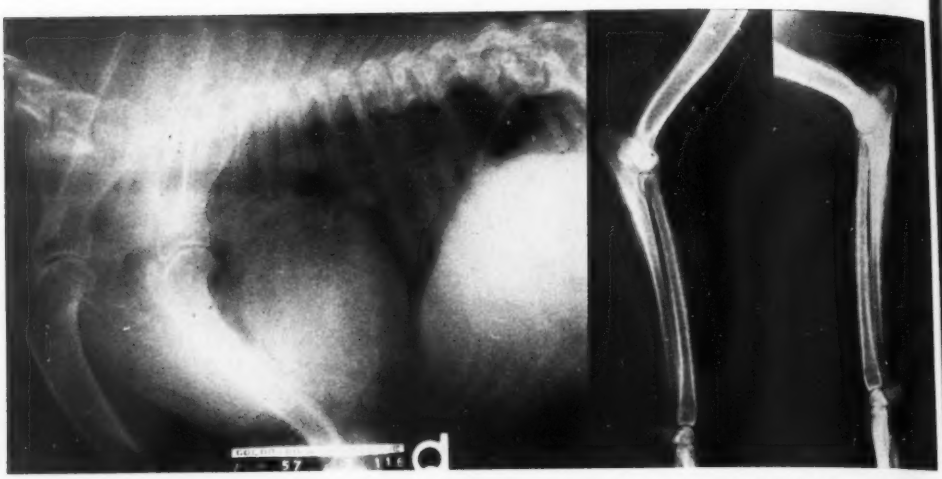


Fig. 18. Hypertrophic pulmonary osteoarthropathy in a dog. A lung tumor is visualized anterior to the diaphragm and above the cardiac silhouette. Extensive changes are seen in the bones of the right and left forelegs.

Fig. 19. Prostatic enlargement in a dog. The rounded shadow seen near the mid-portion of the abdomen is the urinary bladder which is displaced anteriorly by the markedly enlarged prostate gland.

inlet and the esophagus has been described in the stomach of a dog. Intestinal obstruction may result. Foreign bodies are also often encountered in cattle. In the latter animals, wires and other sharp metallic foreign bodies may perforate the intestinal tract and cause severe problems. This condition is popularly known as "hardware disease."

Foot rot is mentioned in this paper because it is a world-wide problem in cattle and sheep, though extremely un-

common in man. It is an infectious arthritis. Figure 15 shows a rather minor case at the distal interphalangeal joint of a cow, and Figure 16 much more severe involvement in an interphalangeal joint of a cow. Note the cloven hoof or the two toes of this cow as compared with the one toe of the horse. This disease may cause severe debilitation in cattle.

The condition variously known as cardiospasm, achalasia, and esophageal paralysis is approximately as common in dogs as in man (Fig. 17) and in appearance seems to be identical in the two species. We have not encountered it in cats and do not recognize it in larger animals such as horses and cows.

Hypertrophic pulmonary osteoarthropathy is seen occasionally in the dog, where the bony proliferation is extremely widespread and clearly visualized. It is usually associated with a lung tumor. In Figure 18, the tumor is visualized and the periosteal changes on the foreleg are clearly demonstrated. We have not observed the condition in cats or in larger animals such as horses and cows.

Prostatic hypertrophy is relatively common in older dogs (Fig. 19). It is rare that a direct surgical approach is used. Removal of the testicles results in complete cure in a period of three or four months.

SUMMARY

Examples have been presented of pathologic conditions that occur in both animals and man. Intestinal obstruction in the dog, intussusception, osteogenesis imperfecta, cystic calculi, cardiospasm, and hypertrophic pulmonary osteoarthropathy, as well as many other conditions, are, to all intents and purposes, identical in animals and man. We believe that this represents a reservoir of cases with potent opportunity for clinical investigation.

Suite B-208 South College Ave.
Fort Collins, Colo.

SUMMARIO IN INTERLINGUA

Conditiones Morbide in Animales con Constatationes Radiographic Que Etiam Occurre in Humanos

Iste communication presenta e discute brevemente certe exemplos de morbos que occurre in animales si ben como in humanos. Multes de istos es si quasi-identic in animales e humanos que il es difficile distinguer los tanto in lor etiologia como etiam in lor pathologia. Le conditiones discutite include obstruction intestinal, intussusception, pneumonia, ulcere peptic, hernia diaphragmatic, actinomycosis, osteogenese imperfecte, calculos cystic, cardiospasmo, corpores alien, hypertrophic osteoarthropathia pulmonar, putriditate de pede (que es un infectiose arthritis occurrente in bestial e oves), e hypertrophia prostatic.

Es opinate que iste morbos que occurre in animales forni assi un reservoir de casos de interessante possibilitates pro le investigation clinic.

EDITORIAL

Arteriomesenteric Occlusion of the Duodenum: An Entity?

The syndrome caused by occlusion of the third portion of the duodenum by the superior arteriomesenteric vessels was launched by Rokitansky a century ago. It is fitting that the product of so illustrious a sponsor, in view of its many vagaries along the road of professional acceptance, be evaluated again as it begins its second century. According to who is consulted, it should be "relegated to history" or diagnosed much more often than it is.

The sufferers from arteriomesenteric occlusion of the duodenum are commonly young, hyposthenic, lordotic females, often unmarried. It occurs with disturbing frequency in nurses and doctors' wives. This relationship to the medical profession might suggest more or less subtle pressures upon clinicians, radiologists, and surgeons to produce a socially and medically acceptable organic basis for the troubles that affect their own. The unmarried status of so many patients has been explained on the basis of the chronic disease making young women unsuitable candidates for the trials of marriage; I find it equally likely, however, that their unsuitability for these trials is just another manifestation of an unstable psychologic or neurovegetative constitution.

The frequency and severity of "toxic" symptoms of headache and vertigo in the recorded examples of the syndrome, as contrasted with their absence in the truly organically determined aganglionosis of the duodenum, must lead us to doubt that patients with these complaints represent true examples of arteriomesenteric duodenal occlusion.

Functional dilatation of the duodenum as a reflex from diseases in the gastrointestinal tract itself (especially peptic ulcer or gastritis), biliary tree, pancreas, and distant organs, is far commoner than dilatation from all the mechanical causes put together (bands, adhesions, intrinsic and extrinsic tumor, arteriomesenteric occlusion, etc.). Diminution in caliber of the duodenojejunal segment, and visible and palpable indentation of the superior mesenteric artery upon the anterior surface of the duodenum are normal findings. Obviously, this indentation becomes deeper, the more the duodenum becomes dilated. It is this mechanism, I believe, that has given rise to most of the diagnoses of arteriomesenteric occlusion made at the operating table; the role of the superior mesenteric artery is, in fact, circumstantial (*circumstare*, to stand around).

This diagnosis cannot possibly be offered without radiologic support. Many of the radiologic observations in the proximal duodenum upon which the diagnosis has been made, however, such as vigorous to-and-fro peristalsis, delay and puddling of the barium especially in the supine hyposthenic patient, an apparently sharp cut-off or narrowing of the caliber a little to the right of the spine, regurgitation of barium into the stomach, all have been repeatedly shown to be normal findings. When the radiologist is confronted with a striking dilatation in the proximal duodenum, it behooves him to put forth his best efforts to uncover peptic ulcer or disease in the surrounding (or distant) viscera before making a diagnosis of arteriomesenteric occlusion. If there is any clinical support at all, I should consider the dilated duodenum—merely on a probability basis—highly suggestive of peptic ulcer or gastritis, even without direct evidence for these.

Findings at the operating table are

often indecisive because of the technical difficulties experienced even by skilled surgeons in examining the third and fourth portions of the duodenum completely. A good postoperative course never proves a diagnosis. The effects of somatic and psychologic pampering, not to mention the endocrine boost incident to the surgery, cannot be minimized. Even the explanation of a large duodenum furnished by autopsy may be indecisive because of the dynamic nature of arteriomesenteric occlusion.

Doubt is widespread that surgical measures alone are adequate in treatment of this condition; medical, postural, and even psychotherapeutic adjuncts may be needed. This is incomprehensible in a truly organically determined occlusive syndrome: elsewhere along the intestinal tube, surgery for simple obstruction is a totally curative measure.

Is arteriomesenteric occlusion of the duodenum a true syndrome? From the foregoing, it may be adduced that the syndrome has been considerably over-reported. Nordentoft indicates the middle course between its acceptance and rejection with his sage counsel that additional cases of megaduodenum be collected and studied, and not dismissed with the ready explanation of arteriomesenteric occlusion.

Acute gastric dilatation is a distressingly serious complication of surgery, grave medical conditions, injury with or without the application of a body cast, dietary indiscretion (*e.g.*, rutabagas), or even with no known predisposing factor. As a postoperative complication it has become less common with the newer knowledge of water and electrolyte balance. Rather than a simple occlusive syndrome, acute gastric dilatation must represent a severe disturbance in the autonomic innervation of the stomach and varying increments of the small intestine; motor activity is lost, and there is a massive accumulation of gastric secretion. A similar condition can be produced experimentally. This is a disease *sui generis*, and should not be confused with arteriomesenteric occlusion of the duodenum, despite the attempts in the past to implicate it as a causative or contributory factor.

The interested reader can find elaboration of these arguments with documentation in a recent issue of the *Virginia Medical Monthly*.[1]

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

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[1] CIMMINO, C. V.: The Status of the Syndrome of Arteriomesenteric Occlusion of the Duodenum. A Critical Review. Virginia M. Monthly **88:** 192–204, April 1961.

UNIVERSITY OF ROCHESTER THIRD CINEFLUOROGRAPHY SYMPOSIUM

The Staff of the Department of Radiology at the University of Rochester, N. Y., will hold its Third Symposium on Cinefluorography in Rochester, on Friday and Saturday, Dec. 1–2, 1961. The program will include basic orientation in problems of motion picture radiography as well as demonstrations of the applications of cinefluorography in the basic and clinical sciences.

This announcement is an invitation for the submission of scientific papers dealing with any facet of the technical or applied aspects of motion picture radiography.

The seating capacity of the auditorium will limit registration to approximately 150 persons. Inquiries or applications should be addressed to Stanley M. Rogoff, M.D., Division of Diagnostic Radiology, University of Rochester Medical Center, Rochester 20, N. Y.

POSTGRADUATE COURSE IN OCULAR RADIOLOGY

The Institute of Ophthalmology of the Americas announces a Postgraduate Course in Ocular Radiology, including both diagnosis and radiation therapy, to be offered Oct. 3–Nov. 2, 1961. Details regarding registration and fees may be obtained from Mrs. Tamar Weber, Registrar, Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary, 218 Second Ave., New York 3, N. Y.

RADIATION COURSES QUEENS HOSPITAL CENTER, NEW YORK

Three radiation courses will be given this coming autumn at the Queens Hospital Center, Jamaica, N. Y.: a one-week intensive course on Specialized Radiation Procedures in the Treatment of Cancer, beginning Oct. 16, 1961; a Wednesday morning course in Operative Radium Therapy, 9 A.M. to noon, Oct. 4 to Nov. 22; a Wednesday afternoon course in Radioactive Isotopes for Technicians for 8 sessions of four hours each, 1 to 5 P.M., beginning Sept. 27, 1961.

Enrollment for these courses is limited. The tuition fees are $150.00 for the course on the treatment of cancer and $100.00 for each of the other two courses. Requests for applications for each course should be sent to Dr. Philip J. Kahan, Supervising Medical Superintendent, Queens Hospital Center, 82–68 164th St., Jamaica 32, N. Y.

THIRD INTERNATIONAL CONVENTION OF X-RAY TECHNICIANS

The Third International Convention of X-Ray Technicians, sponsored by the Canadian Society of Radiological Technicians and the American Society of X-Ray Technicians, will be held at the Queen Elizabeth Hotel, Montreal, Quebec, Canada, June 24–29, 1961, as previously announced in RADIOLOGY.

The Workshop Refresher Courses, scientific papers, and technical exhibits are all designed to keep technicians abreast of current trends and new developments in their field. The memory of two pioneers in technology will be honored Thursday, June 29, with the presentation of the Jerman Memorial Lecture by Richard Olden, R. T., Baltimore, Md., and the Welch Lecture by Guillaume Gill, M.D., Montreal, Quebec.

BROOKHAVEN SYMPOSIUM IN BIOLOGY

The annual summer conference sponsored by the Biology Department of Brookhaven National Laboratory, Upton, N. Y., will take place June 5–7, 1961. The subject of this year's symposium is "Fundamental Aspects of Radiosensitivity."

ERRATUM

The authors of the paper "Radiophotoluminescent Gamma-Ray Dosimetry of Mixed Neutron Gamma-Ray Radiation Fields" in RADIOLOGY for February 1961 (**76:** 290, 1961) have asked that a correction be made in Equation 1 and the four lines following it and in Equation 2, so that these will read:

$$ED = N\sigma\phi\bar{E}_B A w^{-1}\, 1.6 \times 10^{-24} \qquad (1)$$

where

N = the number of silver target nuclei per needle
σ = average thermal activation microscopic cross section in barns
ϕ = the time integrated thermal neutron flux in n/cm^2: (this term can also be called NVT)

$$ED = N\sigma\phi\bar{E}_B A w^{-1} \lambda \int_0^t e^{-\lambda t} dt\, 1.6 \times 10^{-24} \qquad (2)$$

INTERNATIONAL CANCER FELLOWSHIPS

The International Union Against Cancer, through funds made available by the Eleanor Roosevelt Cancer Foundation, will annually award fellowships for research on cancer. These will be senior postdoctoral awards to full-time staff members of universities, teaching hospitals, research laboratories, or other institutions, who have demonstrated outstanding ability or promise as independent investigators in the field of research on basic cancer, its experimental and clinical aspects, and who wish to broaden their experience by a period of study in another country. The stipend will be based on the current salary of the applicant and the salary of persons of comparable qualifications in the place

where the applicant expects to study. An allowance will be made for dependents and for travel costs.

Application forms and additional information may be obtained from International Union Against Cancer, P. O. Box 400, Geneva 2, Switzerland.

Letter to the Editor

Dr. Howard P. Doub, Editor

DEAR DR. DOUB:

Dr. Cimmino's editorial in the January issue on "Statistics and the Physician" is meant to be provocative. I'm already sensitized by a current endeavor to write an essay on common sense. I hope we can all agree with Cimmino that the quoted motto, "Figures don't lie, but liars [sure do] figure" is to be classed as a "snide remark." His second motto, "You can prove anything with statistics," should be parried with "You can prove anything by anecdotes." Each is a good, serviceable *caveat.*

Radiologists should be physicians ("first a physician!"). Before this becomes a sterile cliché that excites only partisan approbation, but no thought, we should confess the semantics and the teleology. It means that a radiologist should have understanding that encompasses all of medicine, not just a segment of it. It exhorts the radiologist to practice the medical art, while implying that he is likely to be doing something else. Indeed, he is—he is consulting with his fellow physicians and giving them advice. This is not something done to the patient, it is something communicated from one mind to another, *i.e.*, science.

In a world of infinite variety, how can a man, with finite mind, keep from being infinitely surprised? Why, by abstracting a finite set of uniformities and dealing with those. With experience only of yesterday and a look at only a tiny corner of the world, how predict the next bit that he will see tomorrow? Why, by assuming that the world he will see is the same world he has seen.

He will be seeing things and events such as he has seen before. Those features and relations (abstractions) that he has seen (and measured) a number of times and found uniform, he expects to find the same again. Mathematics provides a language in which he can state his magnitudes and relationships with perfect clarity. The operations of mathematics serve to reveal other ways of saying the same thing (tautologies) and so making him aware of applications that he might otherwise overlook. This is fine when we do have experience of uniformity in multiple observations. But what about multiple observations enough alike to be classed together but obviously different one from another in some respect. When the differences in a feature are measurable or countable, we can deal with two abstractions, namely the invariant part and the variability *per se.* The mathematics for handling the magnitude of the invariant part (the central tendency) and the variability (deviations from the central measure) is statistics. Statistics makes use of ordinary mathematical operations. It proceeds on the conviction already stated that it is always the same old world. But statistics sets forth not only the uniformities but also the variations, expecting both uniformities and variations in the world we have not yet seen to be the same as in the world we have already seen (and measured).

I don't see why so many people have little confidence in the projection of variability when they show plenty of confidence in the projection of uniformity. It looks like a hunger strike without anything to strike for. Either they deny themselves the use of observations that are not absolutely uniform (and what observations are?), or else they ignore the variations, which then inevitably gang up to plague them.

It's time we made up our pedagogic mind to teach variance at the same time we teach averages.

Sincerely,

R. R. NEWELL, M.D.

In Memoriam

FRANKLIN BLEVINS BOGART, M.D.

1894–1961

Franklin Blevins Bogart, M.D., was born in Chattanooga, Tenn., May 15, 1894, spent most of his life in the practice of radiology in that city, and died there on March 11, 1961. He came of a family of physicians, being the son of Dr. W. M. Bogart and the grandson of Dr. Franklin Bogart. An uncle, also, was engaged in the practice of medicine.

Dr. Bogart received his B.S. and M.S. degrees from the University of Wisconsin, in 1916 and 1917, and his M.D. from Johns Hopkins in 1919. He was in the army briefly in 1917 and again in 1942 to 1945, as Major and later Lieutenant-Colonel in the Medical Corps. He served as Chief of the Radiological Service of Letterman General Hospital, San Francisco.

Dr. Bogart was a diplomate of the American Board of Radiology, a fellow of the American College of Radiology, and a member of the Radiological Society of North America, the American Roentgen Ray Society (First Vice-President in 1958–59), and the American Radium Society. In addition to his private practice he held the following appointments: Radiologist, Pine Breeze Sanatorium; Co-Director, Chattanooga Tumor Clinic, Erlanger Hospital (oncology); Consulting Member of the Staff of Memorial Hospital and State Tuberculosis Hospital, Chattanooga. He served his county medical society as vice-president and president in 1933 and 1934 and was president of the Tennessee State Medical Association in 1947–48. His published work included some twelve or fifteen papers appearing in the *Tennessee State Medical Journal, The Southern Medical Journal,* RADIOLOGY, and the *American Journal of Roentgenology.*

Dr. Bogart was a member of the Lookout Mountain Presbyterian Church. His wife, the former Rose Alice Harloff, whom he married in 1920, and two daughters, Helen Keturah (Mrs. David S. Smith) and Alice Jane, survive him.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

PEDIATRIC X-RAY DIAGNOSIS: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS OF PEDIATRICS, SURGERY & RADIOLOGY. By JOHN CAFFEY, A.B., M.D., Director of Medical Education, Children's Hospital of Denver; Consultant Pediatrician, National Jewish Hospital at Denver, Colo.; Professor Emeritus of Radiology, College of Physicians and Surgeons, Columbia University; Consultant Radiologist, Columbia-Presbyterian Medical Center, New York, N. Y. A volume of 1,236 pages, with 2,908 illustrations on 1,536 figures. Published by Year Book Publishers, Inc., Chicago 11, Ill , 4th ed., 1961. Price $32.00.

THE PHYSICS OF RADIOLOGY. By HAROLD ELFORD JOHNS, M.A., Ph.D., F.R.S.C., LL.D., Professor of Physics and Professor of Medical Biophysics, University of Toronto; Head, Physics Division, Ontario Cancer Institute, Toronto, Canada. Publication No. 419, American Lecture Series. A volume of 768 pages, with numerous figures and tables. Published by Charles C Thomas, Springfield, Ill., 2d ed., 1961. Price $23.00.

SIMULTANEOUS BILIGRAPHY: TECHNIC AND INTERPRETATION. A REFRESHER COURSE. SECTION ONE: RADIOGRAPHY OF THE INTACT EXTRAHEPATIC BILIARY TRACT. By OSCAR M. WEAVER, JR., M.D., D.A.B.R., Stevens Clinic Hospital, Welch, W. Va. A loose-leaf syllabus of 138 pages, with figures. Published by the Author, 1960. Additional copies may be obtained from Superior Office Supply, Inc., Department S-60, Box 591, Welch, W. Va.

SURGERY OF THE ESOPHAGUS. By RAYMOND W. POSTLETHWAIT, M.D., Professor of Surgery, Duke University Medical Center; Chief of Surgery, Veterans Administration Hospital, Durham, N. C., and WILL CAMP SEALY, M.D., Professor of Thoracic Surgery; Chief, Division of Thoracic Surgery, Department of Surgery, Duke University Medical Center, Durham, N. C. A volume of 482 pages, with 200 figures. Published by Charles C Thomas, Springfield, Ill., 1961. Price $30.00.

RADIOISOTOPE TECHNIQUES IN CLINICAL RESEARCH AND DIAGNOSIS. By N. VEALL, B.Sc., F.Inst.P., Guy's Hospital Research Fellow; Honorary Research Physicist, Institute of Obstetrics and Gynaecology, University of London, London, England; Consultant Physicist, Plastic Surgery Centre, Salisbury, and H. VETTER, M.D., Head, Radioisotopes Laboratory, 2nd Medical University Clinic, Allgemeines Krankenhaus, Vienna, Austria. A volume of 418 pages, with 74 figures. Published by Butterworth, London, England, and Washington 14, D. C., 1958. Price $10.00.

ANATOMY AND PHYSIOLOGY FOR RADIOGRAPHERS. By C. K. WARRICK, M.B., B.S. (Lond.), M.R.C.S., L.R.C.P., F.R.C.S.(E), F.F.R., D.M.R., Consultant Radiologist, Royal Victoria Infirmary, Newcastle upon Tyne and Lecturer in Radiological Anatomy, University of Durham, Durham, England. A volume of 266 pages, with numerous figures. Published by Edward Arnold Ltd., London, England, 1960. Exclusive U. S. agents, The Williams & Wilkins Co., Baltimore, Md. Price $7.00.

THE SPECTRA OF X RAYS SCATTERED IN LOW ATOMIC NUMBER MATERIALS. By W. R. BRUCE, M.D., Ph.D., Physics Division, Ontario Cancer Institute, Toronto, and Assistant Professor of Medical Biophysics, University of Toronto, Canada, and H. E. JOHNS, Ph.D., F.R.S.C., Physics Division, Ontario Cancer Institute, Toronto, and Professor of Physics, University of Toronto, Canada. (Formerly Professor of Physics, University of Saskatchewan.) This work was performed while the authors were with the Physics Department, University of Saskatchewan, Saskatoon, Sask , Canada. British Journal of Radiology Supplement No. 9. A monograph of 58 pages, with figures and tables. Published by the British Institute of Radiology, London, England, 1960. Price $2.00.

DEPTH DOSE TABLES FOR USE IN RADIOTHERAPY. A SURVEY, PREPARED BY THE SCIENTIFIC SUB-COMMITTEE OF THE HOSPITAL PHYSICISTS' ASSOCIATION, OF CENTRAL AXIS DEPTH-DOSE DATA MEASURED IN WATER OR EQUIVALENT MEDIA. British Journal of Radiology Supplement No. 10. A monograph of 96 pages, with figures and tables. Published by the British Institute of Radiology, London, England, 1961. Price $7.50.

CANCER: PROGRESS VOLUME 1960. Edited by RONALD W. RAVEN, O.B.E.(MIL.), T.D., F.R.C.S., Joint Lecturer in Surgery, Westminster Medical School, University of London; Surgeon, Westminster Hospital Teaching Group; Surgeon, The Royal Marsden Hospital, London; Surgeon, The French Hospital, London. A volume of 258 pages, with 45 figures. Published by Butter-

worth, London, England, and Washington 14, D. C., 1960. Price $12.00.

LES CHONDRODYSTROPHIES GÉNOTYPIQUES. By MAURICE LAMY, Professeur de clinique de génétique médicale à la Faculté de médecine de Paris; Médecin de l'Hôpital des enfants malades, and PIERRE MAROTEAUX, Chef de laboratoire à l'Hôpital des enfants malades; Chargé de recherches au Centre national de la recherche scientifique. A monograph of 120 pages, with 100 figures. Published by L'Expansion scientifique française, 15, rue Saint-Benoît, Paris VI,° France, 1960. Price 10 NF.

DIE MYELOGRAPHIE MIT POSITIVEN KONTRASTMITTELN. By Priv.-Doz. Dr. med. J. WELLAUER, Zürich. With a foreword by H. R. Schinz, Prof. Dr. med. Dr. rer. nat. h.c., Zürich. Ergänzungsband 89, Fortschr. a. d. Geb. d. Röntgenstrahlen. A monograph of 176 pages, with 294 illustrations on 172 figures. Published by Georg Thieme, Herdweg 63, (14a) Stuttgart, Germany, 1961. Distributed in the United States and Canada by Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 54.—($12.85); to subscribers to the Fortschritte, DM 48.60 ($11.55).

DOSIMETRIE DER STRAHLUNGEN RADIOAKTIVER STOFFE. By Dr. phil. WALTER MINDER, ao. Professor für medizinische Strahlenphysik an der Universität und Leiter des Radium-Institutes in Bern. A volume of 300 pages, with 137 figures. Published by Springer, Mölkerbastei 5, Vienna I, Austria, 1961. Price $15.25.

Book Reviews

TUMORS OF CHILDHOOD: A CLINICAL TREATISE. By HAROLD W. DARGEON, M.D., Attending Pediatrician and Chief, Pediatric Service, Memorial Hospital for Cancer and Allied Diseases; Attending Pediatrician, St. Luke's Hospital; Associate Professor of Clinical Pediatrics, Cornell University Medical College, New York, N. Y. A volume of 476 pages, with 315 figures. Published by Paul B. Hoeber, Inc., Medical Division of Harper & Brothers, New York 16, N. Y., 1960. Price $20.00.

This work is designed primarily to present the subject of juvenile tumors from the standpoint of the clinician. It is an excellent presentation of the clinical aspects of these tumors, the various means of diagnosis and treatment, and the prognosis. The text is divided into two main parts: Part I, which is relatively brief, presents many of the basic facts concerning the etiology, genesis, classification, incidence, and sites of childhood tumors in general. Part II, comprising the main body of the work, deals with specific neoplasms, classified mainly according to the most frequent anatomic site of occurrence.

The clinical descriptions are relatively short, but the main features of diagnosis and treatment are described. The radiographic changes are given in capsule form but are satisfactory for a clinical treatise. The radiotherapeutic aspects are given some attention but their coverage leaves much to be desired by the trained radiotherapist. The text is well illustrated by photographs and radiographs.

This book will be of special value to pediatricians, surgeons, and students rather than to radiologists.

THE YEAR BOOK OF CANCER (1959–1960 YEAR BOOK SERIES). Compiled and edited by RANDOLPH LEE CLARK, JR., B.S., M.D., M.Sc. (Surgery), D.Sc. (Hon.), Houston, Texas, Director and Surgeon-in-Chief, The University of Texas M.D. Anderson Hospital and Tumor Institute; Professor of Surgery, The University of Texas Postgraduate School of Medicine; Clinical Professor of Surgery, Baylor University College of Medicine; Chairman, Committee on Cancer, American College of Surgeons; F.A.C.S., and RUSSELL W. CUMLEY, B.A., M.A., Ph.D., Houston, Texas, Director of Publications, the University of Texas M.D. Anderson Hospital and Tumor Institute; Professor of Medical Journalism, The University of Texas Postgraduate School of Medicine; Executive Editor, Medical Arts Publishing Foundation. A volume of 534 pages, with 172 figures. Published by the Year Book Publishers, Inc., Chicago 11, Ill., 1960. Price $8.50.

The voluminous literature on oncology is such that it is a mammoth task to select the articles for inclusion in an annual compilation such as is contemplated in the well known *Year Book* series. The editors of the *Year Book of Cancer* have again enlisted a board of physicians and scientists to assist in this undertaking, their assignments covering nineteen different aspects of the cancer problem, from anesthesiology to urology. If to these are added the authors of the original papers, who have assumed the responsibility of preparing abstracts of their individual contributions, the number of persons who have helped in getting out this book comes to a total of some 470.

The contents of the volume are divided into twenty-six sections, of which about half are devoted to the different anatomic parts of the body. The other sections relate to diagnostic measures, therapeutics, care of the patient, biology, physics, etc. A special chapter deals with "Clinical Staging of Cancer for End-Result Reporting," and another with "Smoking—The Cancer Controversy."

The abstracts are well chosen and very complete. The reader is given an excellent review of the original article and in many instances the editors have added a thumbnail opinion.

This book is most valuable for anyone who is interested in any aspect of oncology.

LUMBAR DISCOGRAPHY AND LOW BACK PAIN. By DONALD DEFOREST BAUER, M.D., C.M., M.Sc., Consulting Radiologist, Klamath Valley Hospital and Hillside Hospital; Associate Supervisor and Radiologist, Department of Medical X-Ray Technology, Oregon Technical Institute, Klamath Falls, Ore. A monograph of 90 pages, with 32 figures. Published by Charles C Thomas, Springfield, Ill., 1960. Price $5.00.

In this short monograph the author makes a strong case for discography. He indicts myelography as giving only indirect evidence of herniation of the disks, and then only of the posterior ones. Discography is portrayed as being the only method capable of proving that a disk is normal. It also demonstrates anterior, lateral, posterior, and vertical herniation and shows whether the posterior longitudinal ligament or the annulus is torn.

Chapters are devoted to the technic of discography and its practical application, including its research and legal values. Numerous radiographs portray its usefulness in various pathologic conditions.

This monograph will furnish a valuable review to those who are interested in this subject. It should be noted, however, that the procedure has not won universal acceptance.

QUADRI RADIOLOGICI DELLE PNEUMOPATIE INTERSTIZIALI IDIOPATICHE E SISTEMICHE NELL'ADULTO. By E. BALESTRA, Istituto di radiologia dell'Università di Genova. A monograph of 196 pages, with 63 figures. Published by Edizioni Minerva medica, Turin, Italy, 1960.

In this book the author discusses a very difficult chapter of pulmonary pathology and attempts to explain radiological appearances on the basis of the anatomicopathological alterations. In his introduction he states that a distinction must be made between pulmonary fibrosis and the active processes of the interstitial pulmonary tissue. He also seeks to distinguish fibrosis from sclerosis, sclerosis implying an atrophic process of the fibrous tissue. Several pages are devoted to the various classifications of interstitial diseases of the lungs proposed by Vallebona, Mazzini, Antoniazzi, Daddi, and Spain.

The pathological findings in interstitial pneumopathies are given as follows: (1) cellular infiltration of the interstitial tissue; (2) interstitial edema; (3) secondary alteration of alveolar epithelium; (4) nodular formations due to endo-alveolar fluid, to circumscribed atelectasis, to cellular infiltration, or to fibrotic changes; (5) microcystic formations in chronic forms; (6) bronchiectatic and microbronchiectatic formations; (7) alterations of the lymph nodes; (8) alterations of the blood vessels.

The radiological changes are given as follows: (1) accentuation of the normal pulmonary markings; (2) nodular formations; (3) limited segmental atelectases; (4) multiple radiolucent areas due to air cysts and bronchiectases; (5) alterations of the lymph nodes; (6) alteration of the vasculature.

Following these general considerations, there are discussions of the specific pathology and the radiological appearance of The Hamman-Rich syndrome, of interstitial chronic pneumopathy with micro-polycystic transformation, of involvement of the lungs in generalized collagen diseases, in granulomatous and leukemic conditions, in virus infections, in pulmonary edema, and in uremia.

In the differential diagnosis the author discusses the interstitial tissue involvement in syphilis, in tuberculosis, as a reaction to retained Lipiodol, following therapeutic radiation, in allergy, in chronic bronchitis, in bronchiectasis, in fungous infection, in silicosis, in asbestosis, in berylliosis, in pulmonary hypertension, in diffuse pulmonary adenomatosis, in endo-alveolar microlithiasis, and in sarcoidosis.

This book, like other works on the same subject, leaves the reader perplexed by the great variety of radiological aspects which can be produced by the so-called interstitial diseases of the lungs. The reviewer believes that, in view of the difficulties of radiological diagnosis, lung biopsies should be used more frequently.

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

The Roentgen Diagnosis of Intracranial Incisural Space Occupying Lesions. Juan M. Taveras. Am. J. Roentgenol. **84**: 52–69, July 1960. (622 West 168th St., New York 32, N. Y.)

The tentorial incisura is a rigid, roughly oval opening, circumscribed anteriorly by the dorsum sellae, laterally and posteriorly by the edge of the tentorium. The upper portion of the brain stem occupies most of the available space; in addition, the incisura contains the upper portion of the basilar artery with its bifurcation as well as the two posterior cerebral and superior cerebellar arteries and the third and fourth cranial nerves. The tentorial edge is in close relationship to the cerebral peduncles, the quadrigeminal plate, the splenium of the corpus, and the vein of Galen.

Masses occurring in the region of the incisura are usually extracerebral in origin, and the majority can be removed surgically. Because of the possibility of injury to vital areas of the brain, any attempt to remove these lesions must be based on a very accurate preoperative anatomic diagnosis. The lesion must be evaluated as to size, exact location in relation to the brain stem, the edge of the tentorium, the middle fossa, and the major arterial trunks. This can usually be accomplished roentgenologically. The author presents the findings in 14 patients with lesions of the incisura and analyzes the roentgen features. The cases were divided into five groups, depending upon the relationship of the mass to the midbrain: midline anterior, anterolateral, lateral, posterolateral, and midline posterior. The series included 16 meningiomas, 5 aneurysms, and 3 chordomas.

In the majority of patients with an extra-axial incisural mass, pneumoencephalography is the procedure of choice. Cisternal as well as ventricular fillings are easily obtained, with no danger to the patient if performed carefully. In the author's series ventriculography was performed only in the presence of severe increased intracranial pressure (3 cases) or when no ventricular filling was accomplished by pneumoencephalography (2 cases). Vertebral angiography and sometimes also carotid angiography are required if the possibility of a vascular lesion is raised. Angiography is particularly important in the midline anterior lesions, not only because many of them are basilar artery aneurysms, but also because the posterior displacement of the basilar artery is diagnostic of an extra-axial mass.

In most of the cases, except those in the midline group, the postero-inferior portion of the third ventricle showed a fairly characteristic indentation as seen in the anterior projection, and the aqueduct was displaced laterally.

Thirty-nine roentgenograms; 3 diagrams.

P. F. CHRISTENSON, M.D.
Fontana, Calif.

Emulsified Iodized Oil Ventriculography. Toshio Matsubara and Takayoshi Nomura. Am. J. Roentgenol. **84**: 48–51, July 1960. (Nagoya University School of Medicine, 65, Tsurumai-cho, Showa-ku, Nagoya, Japan)

Delineation of the third and fourth cerebral ventricles and the sylvian aqueduct is often inadequate when conventional pneumoventriculography and Lipiodol ventriculography are employed, since air and Lipiodol are not miscible with the cerebrospinal fluid. Unless the contrast material spreads through the ventricular space, independent of external factors, the result will vary with the technic used. After much experimentation, the authors have found a way to emulsify iodized oil, which renders it diffusible with the cerebrospinal fluid.

Four parts of isobaric iodized oil and 1 part of a neutral isotonic solution of sodium lauryl sulfate are mixed and vigorously shaken, to produce emulsification. The method of preparing the solution of sodium lauryl sulfate is described. The iodized oil is a molecular uniform isobaric Lipiodol (11.63 per cent iodine content), the specific gravity of which is 1.005–1.007 at body temperature, similar to that of normal cerebrospinal fluid.

A unilateral ventricular puncture is made into the anterior horn of the lateral ventricle, with the tip of the needle directed at the foramen of Monro. Ten to 20 milliliters of cerebrospinal fluid is removed and replaced by the same amount of the emulsified iodized oil, which is injected slowly into the ventricular space. Soon after the injection (within several minutes) ventriculograms are taken from various directions, without removing the needle. When the desired information has been obtained, the contrast material is removed by irrigation of the cerebrospinal spaces with artificial cerebrospinal fluid or with Ringer's solution at body temperature.

The advantages of emulsified iodized oil ventriculography are as follows: (1) The entire ventricular system is visualized, since the contrast medium diffuses through the cerebrospinal fluid. (2) The narrow part, the third and fourth ventricles, and the sylvian aqueduct, can be demonstrated without troublesome screening or changing the position of the patient's head. (3) The contrast substance can be removed by irrigation.

The results of emulsified iodized oil ventriculography in 14 patients are presented in tabular form. Side reactions have consisted of temporary fever, slight headache, and, infrequently, nausea and vomiting, which were relieved without medication.

Three roentgenograms.

P. F. CHRISTENSON, M.D.
Fontana, Calif.

Cerebral Angiography in the Diagnosis of the Acute Stroke. J. W. D. Bull, John Marshall, and D. A. Shaw. Lancet **1**: 562–565, March 12, 1960. (The National Hospital, Queen Square, London, W. C. 1, England)

The contribution of cerebral angiography to the determination of the site and nature of lesions giving rise to an acute stroke was assessed in 80 consecutive patients admitted to the National Hospital (London) and examined angiographically within seventy-two hours of the onset of the stroke.

In 33 cases (41 per cent) evidence of a specific lesion was disclosed, in 46 no abnormality was detected, and in 1 vertebral angiography was unsuccessful. Occlusion of the internal carotid artery was demonstrated in 14 cases (complete in 10 and partial in 4); only 4 of these cases had been diagnosed clinically. Eight patients had occlusion of the middle cerebral artery, all at the classical site just proximal to the bifurcation or trifurcation of the main vessel; in 3 of this group the clinical diagnosis was cerebral hemorrhage and in a fourth it was internal carotid occlusion. Angiography revealed oc-

clusion of the basilar artery in 2 cases, in both paradoxically by the carotid route. Intracerebral hemorrhage was diagnosed angiographically in 6 cases, in only 4 of which had the diagnosis been made clinically. In a further case, angiography showed intracerebral hemorrhage that had arisen from a ruptured aneurysm.

Taking the figures as a whole, 16 of the 33 positive angiograms confirmed the clinical diagnosis, while 17 showed it to be incorrect. Thus, in 17 of the 80 cases (21 per cent) angiography was an essential adjunct to diagnosis by revealing lesions undiagnosed by the clinician. In 9 per cent it was helpful by failing to confirm a clinical diagnosis which might otherwise have led to exploration of the neck, and in 20 per cent by giving support to the clinical diagnosis.

Complications arose after angiography in 9 patients, although fortunately these were all transient. As the condition of some patients was deteriorating before angiography, the complication rate of 11 per cent may well overestimate the hazard.

Until the value of the various forms of therapy is known, the place of angiography as a step toward definitive treatment cannot be finally assessed.

Three tables.

Cerebral Angiography in the Rabbit. An Investigation of Vascular Anatomy and Variation in Circulatory Pattern with Conditions of Injection. P. G. Jeppsson and Tord Olin. Lunds Universitets Årsskrift, N. F. Avd. 2. **56:** No. 14, 1960. (University of Lund, Lund, Sweden)

In a small monograph the authors report an angiographic study of the anatomy of the rabbit's brain. The rabbit is a suitable laboratory animal for the investigation of the cerebral circulation since the brain is supplied almost entirely by two internal carotid arteries and two vertebral arteries, as in man. About 70 animals were used in the present investigation, the purpose of which was (1) to devise a roentgen technic for demonstrating the pattern of cerebral vasculature; (2) to study the roentgen anatomy of the vessels; (3) to study the flow pattern of contrast medium injected into the carotid artery.

The internal carotid artery is the first vessel to spring from the dorsal aspect of the common carotid artery. In one-fourth of the animals the internal carotid artery and occipital artery originated from a common trunk.

Between the internal and external carotid arteries was an anastomosis of varying width, connecting the internal ophthalmic artery and the maxillary artery.

As a rule, the rabbit has a well developed circle of Willis, which differs from that in man only in that the anterior cerebral arteries are fused; in man they are connected by a short transverse artery.

The influence of intra-arterial injection rate, injection pressure, and blood pressure on the extent of the arteriogram received special attention. It was found that the number of arteries demonstrated increased with the rate of injection; and when the rate was high, the contrast medium passed over into the internal carotid artery, into the vertebral arteries, and into the maxillary artery on the injected side. The number of vascular regions filled increased with the injection pressure. Other conditions being equal, a fall of the blood pressure results in a filling of a larger number of cerebral vascular regions. The relation between the injection pressure and filling of the cerebral vascular regions is expressed better by the difference between the injection pressure and the mean blood pressure (effective injection pressure) than simply by the injection pressure.

Urografin was employed as the contrast medium for angiography. The lowest concentration of the medium capable of producing satisfactory arteriograms on selective injection into the internal carotid artery was 45–60 per cent, corresponding to 0.22–0.29 gm. iodine/ml. The specific gravity of the contrast medium was found to have no demonstrable influence on the filling of the various vessels, as established by changing the position of the rabbit's head during controlled injection.

The anatomy of the venous system of the brain was also studied *in vivo* both by phlebography after initial carotid artery injection and by sinography of the superior sagittal sinus. The blood is drained from the brain mainly by the external jugular system through the temporal emissaries from the transverse sinuses.

The results of the study are briefly discussed in relation to the technic for investigation of the blood-brain barrier.

Twenty-seven roentgenograms; 11 drawings; 6 tables. CHARLES M. GREENWALD, M.D.
St. Cloud, Minn.

An Assessment of the Methods for Determination of the Position of the Pineal Gland in Lateral Skull Roentgenograms. C. B. Lamon and D. G. Wollin. J. Canad. A. Radiologists **11:** 35–39, June 1960. (Toronto General Hospital, Toronto, Ont., Canada)

The following three accepted methods of assessing pineal gland displacement were compared in 155 lateral skull roentgenograms: (1) the method of Vastine and Kinney (as modified by Dyke), in which graphs showing the normal range of pineal position are used; (2) the proportional method of Fray, which is based on the premise that the distance from the inner table of the frontal bone to the pineal gland is 55 to 60 per cent of the anteroposterior distance of the skull, and that the distance from the inner table of the vault to the pineal gland is 51 to 57 per cent of the vertical diameter of the normal skull; (3) Fray's cranioangle method, which consists of applying to the lateral skull roentgenograms a transparency on which 2 angles, one of 11° and the other of 8°, are drawn. With this last method, if the vertex of the 11° angle is placed at the tuberculum sellae with the base line passing through the lambda, a normal pineal gland should fall within the angle above the base line. If the vertex of the 8° angle is placed at the opisthion, with the base line through the bregma, a normal pineal should fall within this angle, posterior to the base line.

All of the patients in the present series had encephalograms, 67 without and 88 with evidence of a space-occupying lesion. Thirty-nine of the 67 patients without signs of a space-occupying lesion exhibited no disease whatsoever and 28 showed ventricular enlargement (probably indicating some degree of cerebral atrophy); in 4 cases the sutures were not well visualized and the pineal position could not be measured by the cranioangle technic. Approximately one-third of the space-occupying lesions produced a displacement of the pineal gland demonstrable by any of the three methods.

None of the methods was entirely satisfactory, but the cranioangle method of Fray is considered best because it gives the fewest false-positives; its one disadvantage is that it cannot be used in about 10 per cent of cases because the bony landmarks are obscure. Skulls with high vaults cannot be reliably assessed by

this method. No relationship which would allow one to predict a false displacement was discovered.

Two roentgenograms; 3 drawings; 2 graphs.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Injection into the Vertebral Arteria Via the Posterior Route. G. Dolce and G. Ramella. Minerva chir. **14:** 709–710, June 15, 1959. English translation in Panminerva med. **2:** 353–354, July-August 1960. (Istituto di radiologia dell'Università dell'Genova, Italy)

The authors describe a method of injecting contrast material into the vertebral artery *via* the posterior route, which they have adopted as a routine practice. It is said to be fairly easy and free from immediate danger.

The patient is placed in a prone position with the head slightly bent, as for the occipito-fronto-nasal sagittal projection. A vertical line is traced from the external occipital protuberance and the atlantoid line is drawn perpendicular to it, 1.5 cm. below the bimastoid line. A puncture is made on the atlantoid line 3 cm. from the median line in a slightly lateral direction. The needle is introduced for some centimeters so as to meet the transverse apophysis of the atlas, then withdrawn a little and bent upward until the tip enters the vertebral artery. Eight milliliters of Triopac 22 is injected. Local anesthesia is not required.

Good visualization is achieved by means of a small amount of contrast medium as the puncture of a cranial segment avoids the dilution of the agent in a long tract of the vertebral artery.

Three roentgenograms.

Rotational Tomography of the Face. Sydney Blackman. Brit. J. Radiol. **33:** 408–418, July 1960. (Department of Radiology, The Royal Dental Hospital, London, W. C. 2, England)

The author discusses at some length the principles and development of panoramic tomography or pantomography, with special attention to the work of Paatero of Finland (see Absts. in Radiology **64:** 307, 1955, and **66:** 310, 1956; also Soila and Paatero: Radiology **66:** 818, 1956). Under the designation rotational tomography, he describes his own adaptation of these principles to studies of the face.

Rotational tomography is a special form of sectional or differential tomography. In a tomographic system of three components (the x-ray tube, the film, and the object), all the components may be moving provided the center of movement of any two of them remains stationary with relation to the third. The basic principle of rotational tomography is that the angular velocities of a point on the patient and the point on the film on which the image is produced are the same.

The apparatus currently used by the author consists of a simplified dental chair, which is electrically propelled to rotate on a given axis, and a special craniostat suspended from above, with its rotational axis colinear with that of the chair. Alongside the craniostat, and almost touching it, is suspended a disk-like table which carries the film in a cassette fixed to a wooden support. All three units, the dental chair, the craniostat, and the film table, rotate synchronously during a normal exposure at exactly the same speed, the dental chair and the craniostat in a clockwise and the film table in a counterclockwise direction. The x-ray beam is directed as nearly as possible perpendicular to the layer of interest throughout its curvature.

With the patient's head enclosed in the craniostat, a film is placed on the table, at approximately the same distance from the axis of rotation of the table as the perimeter of the face, *i.e.*, the mandible, is from the axis of rotation of the head. If a pencil x-ray beam is directed in this transaxial plane as the craniostat and film revolve, a projection of all points on the mandible, the images of which have a common linear speed with points on the film, will become momentarily stationary with respect to the film and will be recorded on the film as an image of the "circumference" of the object.

Because of the semi-elliptical or parabolic shape of the face, the film has to be curved. The cassette support is made of adjustable wooden hinged supports which can be adjusted to assume the desired shape for each patient. A nylon band holds the film in close contact to the wooden support, which has a lead facing to insure that the image is produced only on the film when it is in its transaxial position nearest to the object. The cassette is made of an opaque plastic material in the shape of a long flat pouch and is lined with a single layer of calcium tungstate crystals.

The x-ray beam issues through a vertical 1.5 mm. slit in a diaphragm around the tube. A rotating anode is used with an 0.8 mm. focal spot. The rotating film on the disk table is protected by a stationary curved lead shield which is placed at the periphery of the table. The shield has a vertical slit down its entire length so that the x-ray beam is projected onto the film through this slit, which is about 1 cm. in width. This provides protection from horizontal secondary radiation; protection from vertical secondary radiation is effected by placing a grid in a horizontal position in front of the slit.

The patient is seated in the dental chair with the head in the craniostat and clamped in the sagittal plane. The head is maintained in this position by introduction into the external auditory canals of two small wooden pegs which are attached to two long wooden arms. The distance between the two external auditory canals is used to determine the axis of rotation of the condylar processes of the mandible. The head is further stabilized by two padded compressors. Forward movement of the head increases the extent of the panoramic view from side to side of the face, and retraction of the head confines the arc of examination to the teeth-bearing area of the jaws. The exposure time is twelve seconds and the tube current used is 30 ma. For adults the kilovoltage varies between 80 and 85 and for children from 70 to 75. The dose at the center of radiation averages 0.7 r, while the skin dose is in the neighborhood of 0.17 r.

The author suggests that "rotography" is supplemental to recognized methods of intra-oral and extra-oral radiography. It is not intended to supplant or oust present technics. It is applicable for most surveys and examinations where a simple and rapid means of recording dental conditions and mandibular lesions is required in a large number of people. It may also be used for cephalometric and sinus radiography.

Nine photographs; five radiographs; one table.

HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

Mandibulofacial Dysostosis on the Roentgen Film. J. E. W. Brocher and D. Klein. Fortschr. a. d. Geb. d. Röntgenstrahlen **93:** 67–79, July 1960. (In German) (Universitäts-Augenklinik, Geneva, Switzerland)

Mandibulofacial dysostosis is the commonest form of

dysostosis of the cranial vault. It is characterized by an "anti-mongoloid" position of the eyes and disproportion between the cranium and facial bones. The antra appear abnormally small and flat. The mandible shows marked shortening of the coronoid and condyloid processes, sometimes unilaterally. The external acoustic meatuses may be absent. Pneumatization of the temporal bone, if present, is poor or absent. On the affected side, hearing is usually diminished. Frequently the base of the skull is seen to form a horizontal line.

This condition is said to have its origin in the fourth week of embryonal life. It is frequently associated with other developmental anomalies, as polydactylia and hypodactylia.

In the differentiation from craniostenosis absence of early synostosis is a distinguishing feature.

Thirty-three illustrations, including 26 roentgenograms.

ILONA D. SCOTT, M.D.
Lewisburg, West Va.

THE CHEST

The Problem of Abnormal Radiological Lung Patterns. Josse Kaye and R. Glyn Thomas. M. Proc. (Johannesburg) **6:** 323–332, July 30, 1960. (J. K., Johannesburg Hospital, Johannesburg, Union of South Africa)

A descriptive classification of abnormal radiographic lung patterns is presented, which, it is believed, reduces semantic confusion and will increase the yield of information if it is employed in conjunction with the patient's history, clinical and laboratory investigations, and pulmonary function assessment. Recognition and evaluation of normal or abnormal lung patterns are aided by a radiographic technic including posteroanterior and lateral views in forced inspiration and expiration. These films permit a fairly accurate estimate of the total lung capacity, the vital capacity, and the residual volume. Anteroposterior tomograms are obtained when pulmonary hyperinflation is suspected and axial transverse tomograms in the patient with marked kyphoscoliosis.

In the normal lung pattern, the branches of the pulmonary arteries radiating into the lung fields from the hili can be traced to within half an inch of the chest wall. The veins are not clearly distinguishable from the arteries in the straight chest roentgenogram, except for those draining the right lower lobe. These cross the shadows of the lower lobe arteries almost horizontally near the cardiac silhouette. Causes for pathophysiological modifications of the arterial, venous, and lymphatic shadows, the last normally invisible, are given.

The authors' classification of lung patterns is as follows:

I. Alterations of the Normal Lung Pattern (increased or decreased prominence)
II. Adventitious Pulmonary Patterning
  A. Circular shadows
    1. Granular or punctate (individually invisible; "ground glass" appearance when multiple)
    2. Miliary (up to 4 mm.)
    3. Nodular
  B. Linear shadows
    1. "Hairlines" (*i.e.*, Kerley's B lines; walls of bullae)
    2. "Crayon lines" (thicker lines, clearly distinguishable from blood vessels)
    3. Poorly defined lines
    4. Linear patterns (interlacing or reticulate; discrete)
  C. Combinations of linear and circular shadows.

Sixteen roentgenograms.

PHILIP M. JOHNSON, M.D.
Montclair, N. J.

Roentgen Findings after Pulmonary Surgical Procedures. G. Viehweger. Fortschr. a. d. Geb. d. Röntgenstrahlen **93:** 54–61, July 1960. (In German) (Röntgenabteilung der chirurgischen Universitätsklinik, Würzburg, Germany)

The close co-operation of the surgeon and roentgenologist is required for recognition and treatment of postoperative changes in pulmonary surgery. The author describes and illustrates a few typical complications which may appear on roentgenograms as increased or decreased densities. Their differential diagnosis may be difficult.

Sometimes, following lobectomy, the remaining lobes fail to fill the entire hemithorax and an extrapulmonary hollow space appears. If this cavity remains sterile, there will be no clinical symptoms. If an infection occurs, fistula formation may ensue, opening either internally or externally, or both. Drainage occurs through these fistulas, and on the radiographs no fluid is seen. Often these cavities are mistaken for postoperative reactivation of a specific process. A hollow space can appear also after segmental resection, when the remaining lung fails to expand.

In addition to these extrapulmonary postoperative "cavities," a subpleural "cavity" may appear at the site of the operative field. For the formation of such "cavities" postoperative bleeding and tissue reaction are responsible. After resection the traumatized surfaces lie adjacent to each other. In the fissure which separates them blood and detritus collect. Sometimes this is seen as an increased density. Resorption may occur in a few weeks, but when the necrotic, partially fluid tissue becomes connected with the bronchial system, it will be coughed up; the remaining space will be filled with air; an infection ensues, and a subpleural cavity is formed.

Twelve roentgenograms. ILONA D. SCOTT, M.D.
Lewisburg, West Va.

Pulmonary Aspergillosis with Cavitation Secondary to Histoplasmosis. John J. Procknow and David F. Loewen. Am. Rev. Resp. Dis. **82:** 101–111, July 1960. (University of Chicago School of Medicine, Chicago 37, Ill.)

Several species of *Aspergillus* are capable of causing disease in man. The respiratory tract serves as the most common portal of entry for the organism. The fungus is ubiquitous and grows as a saprophyte in nature. Pulmonary aspergillosis with cavitation may occur as both a primary and secondary infection, clinically and roentgenographically simulating pulmonary tuberculosis. More often it is secondary, superimposed upon antecedent lung disease. The cavitary form of aspergillosis has also been attributed to the protracted use of antimicrobials, corticosteroids, and antineoplastic drugs, as well as to irradiation. The coexistence of aspergillosis with other mycotic infections of the lungs is rather rare.

The authors present what is believed to be the first documented report of pulmonary cavitation caused by the association of histoplasmosis and aspergillosis. The patient, a 28-year-old white male, had an acute febrile episode in September 1956. A chest roentgenogram revealed bilateral apical infiltrates, suggestive of active pulmonary tuberculosis, but the tuberculin skin test was negative. Because a complement-fixation test was positive for *Histoplasma capsulatum* of a 1:4 titer, a diagnosis of acute pulmonary histoplasmosis was considered. By October 1957, the *Histoplasma* complement-fixation titer had fallen to 1:2, and a chest film showed resolution and increasing fibrous scarring in the bilateral apical infiltrates and probable cavitation on the right. The titer of the Histoplasma complement-fixation test fell to negative by January 1959. The patient continued to have cough with debility and was admitted for further study in September 1959. On Sept. 10, the apical and posterior segments of the right upper lobe were removed. Convalescence was complicated by a right bronchopleural fistula, but the patient eventually recovered.

The surgical specimen contained a solitary cavity, the lumen of which contained masses of fungal hyphae; in the lung parenchyma there were granulomas with caseous centers thought to be typical of histoplasmosis. Cultures yielded *Aspergillus fumigatus*, but *Histoplasma capsulatum* was not isolated, nor were any organisms seen in the tissues. Despite this, the diagnosis of histoplasmosis in this patient is believed to be warranted because of the conversion from a negative to a positive histoplasmin skin test in the course of the initial infection, while tuberculin and other fungal skin tests remained negative, and because of the rise and fall in the complement-fixation titer during the course of the initial disease. It is assumed that the *Aspergillus* fortuitously invaded a pre-existing focus of *Histoplasma* infection and overwhelmed the primary agent. The diagnosis of aspergillosis had not been entertained prior to surgery.

Seven roentgenograms; 5 photomicrographs; 1 photograph. JOHN H. JUHL, M.D.
University of Wisconsin

Bronchial Wall Thickening in Asthma. C. J. Hodson and S. E. Trickey. Clin. Radiol. (J. Fac. Radiologists) **11:** 183–191, July 1960. (University College Hospital, London, W. C. 1, England)

The authors state that abnormally thickened bronchial walls are visible on good quality plain chest radiographs. They have investigated the incidence and significance of this finding in 190 patients suffering from asthma. In 121 of these, thickened bronchial walls were found. In 72 cases the thickening was classified as 1 plus, in 45 as 2 plus, and in 4 as 3 plus. Correlation of clinical, radiological, and pathological findings showed that infection was the major etiologic factor in the production of this appearance.

Many patients in the authors' series had been radiographed over a period of years. From an analysis of the films, the conclusion is reached that in the adult asthmatic, once a "thickened bronchial wall pattern" has developed, it will persist as a permanent feature. Although it may wax and wane in its severity, it never clears completely. Its presence may be temporarily obscured during an acute infective episode, but when the acute changes have subsided the thickened walls again become visible.

Since infection appears to be the most important single factor in the causation of this sign, some importance may attach to it as a positive indication for energetic and prolonged chemotherapy, as well as vasodilator drugs, in chronic asthma. The authors also feel that recognition of this sign may help to differentiate cases of "allergic" asthma from those where there is an infective element, and this may lead to earlier and therefore more effective treatment in the latter group. In doubtful cases the presence of thickening can be verified by tomography.

Eight roentgenograms; 4 photomicrographs; 4 graphs; 2 tables. THEODORE E. KEATS, M.D.
University of Missouri

Infrapulmonary Pleural Effusion. Robert A. Flaherty and James M. Keegan. Dis. of Chest **38:** 56–59, July 1960. (R. A. F., 2902 Fairfield Ave., Fort Wayne, Ind.)

The identification of pleural effusion on postero-anterior and lateral chest roentgenograms is usually not difficult. However, when fluid collects between the lung and diaphragm, assuming the contour of the diaphragm without obliterating or blunting the costophrenic sulcus, the appearance may be deceptive. Infrapulmonary pleural effusion should be suspected whenever there is apparent elevation of the diaphragm. Identification of such effusion on the left is facilitated by an increased distance between the gastric bubble and the diaphragm. On the right, fluid is less readily detected because the density is the same as that of the infradiaphragmatic structures.

The presence of an effusion is best demonstrated on the lateral decubitus chest roentgenogram. In this position the fluid will leave its infrapulmonary position and gravitate to the most dependent portion along the lateral costal margin.

In the authors' practice, infrapulmonary pleural effusion is frequently encountered, 19 cases having been seen in a thirty-month period. It has been observed not only postoperatively following thoracotomy but also following thoracic and abdominal trauma and various medical chest conditions. In 3 of the 19 cases the fluid assumed a contour suggesting an apparent lateral shift of the apex of the curve of what seemed to be the diaphragm. Though inconstant, this sign is suggestive of the diagnosis.

Seven roentgenograms; 1 table.
JOHN W. WU, M.D.
Cleveland Metropolitan General Hospital

Bronchography: A Neglected Investigation? W. G. Smith, E. R. Davies, G. S. Lodwig, P. G. Rothwell, and M. P. Mahoney. Lancet **1:** 515–517, March 5, 1960. (Penarth, Glamorgan, Wales)

According to the authors, there seems to be a general impression in Britain that bronchography is a difficult procedure of limited value. They hold a contrary view and describe their technic, step-by-step, to show that bronchography need be neither difficult nor time-consuming. Since it yields vital information not obtainable by other means, especially in bronchial neoplasm, primary and chronic tuberculosis, and bronchiectasis, it should be employed more frequently. Dionosil Aqueous has not been found unduly irritating and provides better contrast and more rapid clearing than the oily suspension.

Two figures.

THE HEART AND BLOOD VESSELS

Differential Diagnosis of the Taussig-Bing Heart from Complete Transposition of the Great Vessels with a Posteriorly Overriding Pulmonary Artery. Alois Beuren. Circulation 21: 1071–1087, June 1960. (Universitätskinderklinik, Göttingen, Germany)

The term "Taussig-Bing transposition" has been applied to two anatomically different malformations. In the *Taussig-Bing heart* (Am. Heart J. **37:** 551, 1949. Abst. in Radiology **54:** 455, 1950), the aorta arises from the right ventricle, but it lies to the right of the pulmonary artery. The pulmonary artery, although in approximately normal position, overrides a ventricular septal defect. There is right ventricular hypertrophy and an anterior deviation of the ventricular septum. A muscular ridge separates the origin of the great vessels. Consequently, most of the venous blood entering the right ventricle is ejected into the aorta and most of the pulmonary blood from the left ventricle is directed into the pulmonary artery. In the *second type* of transposition, the aorta and an overriding pulmonary artery are transposed, but the relation of the two great vessels is very different. The pulmonary artery does not occupy its "approximately normal place" but is far posterior to the aorta. It also overrides a ventricular defect. The aorta arises from the right ventricle, but directly anterior to the pulmonary artery. Thus, in the Taussig-Bing heart the two great vessels are side by side, whereas in the second condition they are completely transposed, *i.e.*, the pulmonary artery lies behind the aorta.

The author reviewed 73 cases of possible Taussig-Bing transposition seen in the Cardiac Clinic of the Johns Hopkins Hospital. In 14 of these, the diagnosis was established by catheterization, angiocardiography, or autopsy. Criteria for the differential diagnosis of these two lesions are pointed out. It rests solely on the relative positions of the great vessels as observed on plain films, fluoroscopy, angiocardiography, and catheterization. Angiocardiography usually gives clear information about the position of the great vessels, the postero-anterior and right lateral views being most helpful. There is usually better opacification of the aorta than of the pulmonary artery. Furthermore, the position of the aorta is so different in the Taussig-Bing heart from that in complete transpositions and in transposition with a posteriorly placed pulmonary artery that differentiation is usually possible. Drawings illustrate the difference in the fluoroscopic appearance of these two transpositions.

[The author states that the differentiation of the two transpositions is of particular importance for possible surgical correction but fails to discuss any significance in this regard. Since the only surgery mentioned is the creation of an artificial septal defect for the all-important admixture of the two circulations, one wonders what the fuss is all about.—Z. F. E.]

Eleven roentgenograms; 4 drawings; 3 tables.

ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Surgical Correction of Aortic Insufficiency Associated with Ventricular Septal Defect. Albert Starr, Victor Menashe, and Charles T. Dotter. Surg., Gynec. & Obst. **111:** 71–76, July 1960. (University of Oregon Medical School, Portland, Ore.)

Although the association of aortic insufficiency with ventricular septal defect is uncommon, the authors were able to find 23 well documented cases available for review with particular reference to the location of the ventricular septal defect and the aortic valve insufficiency. They report 2 additional cases and point out the importance of the recognition of the aortic insufficiency prior to open heart surgery, especially when elective asystole is used as an adjunct. The loss of perfusate into the operative field with resultant drop in perfusion pressure, distention and subsequent damage to the left ventricle, or pulmonary capillary damage resulting from distention of the pulmonary venous circulation may culminate in death. The authors attribute the loss of one of their patients to one or more of these factors.

In the majority of cases the aortic insufficiency is produced by prolapse of the right or posterior cusp, or both, into the left ventricular outflow tract immediately above or through the septal defect. Mere closure of the septal defect may not be sufficient and special attention must be directed to the involved aortic leaflet. A method of correcting the prolapse of the cusp or cusps by suturing the free edge of the involved leaflets is described.

Clinically, this lesion is characterized by a to-and-fro murmur along the left sternal border and a wide arterial pulse pressure. The chest roentgenogram usually shows cardiac enlargement and the increased pulmonary markings of left-to-right shunting. The differential diagnosis includes patent ductus arteriosus with or without ventricular septal defect, aorticopulmonary septal defect, coronary arteriovenous fistula, and ruptured aneurysm of the sinus of Valsalva.

Angiocardiographic studies with injection of contrast material above and below the aortic valve through a spring-guided catheter passed into the aorta through the brachial or femoral artery allow precise diagnosis through visualization of the ventricular septal defect and of the aortic regurgitant jet.

Four roentgenograms; 1 drawing; 2 tables.

FREDERICK J. MUNSON, M.D.
University of Pennsylvania

Dissecting Aneurysm of the Aorta. S. Holesh. Brit. J. Radiol. **33:** 302–310, May 1960. (Kingston Hospital, Surrey, England)

Dissecting aneurysms differ from other aortic aneurysms in that the lumen of the vessel is not enlarged but remains normal or is made smaller by hematoma. The basic cause is a defective media which may be congenital or acquired.

There are two causes of dissecting aneurysms in adults which are thought to be acquired: *Cystic medial necrosis* is the more frequent and is associated with extensive dissection. *Arteriosclerosis* of the intima and media is rare and localized.

Dissection incident to *cystic medial necrosis* always occurs within the media and almost invariably begins in the ascending aorta. Postmortem examination usually shows the intimal rupture in the ascending part of the aorta a few centimeters above the aortic valves, less often in the descending aorta near the isthmus and the ligamentum arteriosum. The most widely accepted view is that medial degeneration with cyst and cleft formation is responsible for intramural hemorrhage which expands, dissects, and secondarily ruptures into the aortic lumen. The dissection may spread proximally and result in aortic valve incompetence or oc-

clusion of the coronary arteries. Usually the spread occurs distally, and all of the aorta and its peripheral branches may be involved. Death frequently follows rupture into the pericardium or extension of the dissection into the coronary arteries. Rupture may occur back into the aortic lumen with formation of a double channel; this is found in the majority of patients who recover. External rupture may occur even after a re-entry.

Arteriosclerotic dissection is seen in an older age group and results from senile sclerosis of the media and atherosclerosis of the intima. Dissection and rupture may occur when circulating blood enters the weakened media through atheromatous ulcers and fissures. Such dissections are usually minimal; if external rupture takes place, it is near the primary intimal lesion. These dissections are more localized and less likely to be fatal than those of the cystic medial necrosis type. The majority of arteriosclerotic dissections are found in the abdominal aorta.

Accurate and prompt diagnosis of dissecting aortic aneurysm is essential, because surgery may be lifesaving. The radiological findings are determined by the stage at which the examination is made. Shortly after the acute phase of the dissection, the whole of the superior mediastinum is widened and the heart is considerably enlarged. The aortic arch is visible but is unsharp and the descending aorta is invisible. A left hemothorax often obscures the left heart border. As recovery takes place, the aortic knuckle becomes more clearly defined and may return to practically normal size. It is, however, usually at a higher level. More often the aorta remains widened and a double aortic knuckle is visible. The dissected portion of the aneurysm is more radiolucent than the dense central core of the aorta, particularly when the dissection involves only the lateral part of the vessel. Dissection is suggested if the thickness of the aortic wall approaches 1 cm.; if it is 1 cm. or more, there is little doubt about the diagnosis.

In chronic cases, the ascending aorta is dilated and the aortic knuckle is abnormally high and prominent, overlapping the shadow of the manubrium. A calcified plaque in the arch region may provide a base line from which to measure the widening of the wall on a series of chest roentgenograms. The dissection often stops just above the hiatus, and a postero-anterior grid film showing a sudden alteration in caliber at this point may be diagnostic.

Angiocardiography is of great value in doubtful cases. Retrograde aortography by the femoral route is considered a safe procedure and is preferred to intravenous angiocardiography because of clearer visualization of the aorta. It will show the lower limit of the dissection and the size of the renal and other vessels in the abdomen. If these are narrowed or not filled, it is an indication that they are involved by the dissection. The most characteristic finding on angiography or aortography is dilatation of the ascending aorta and then narrowing of the caliber, often abruptly, in the transverse and descending portions. If the dissection does not involve the whole circumference, the affected side is irregular and ill-defined. The intercostal arteries on this side are narrowed or absent, whereas the unaffected aortic wall is clearly outlined and regular, and the intercostals are normal. If the dissection has continued into the abdominal aorta, similar changes will be seen, depending on which vessels are involved.

Immediate diagnosis and surgery improve the extremely poor prognosis in patients with dissections. The surgical procedure consists of establishing re-entry of the dissected passage at some distal point into the aorta, as near the origin of the dissection as possible. If the dissection has extended to the abdominal aorta, another re-entry must be made at a lower level to restore the peripheral circulation.

Twelve roentgenograms; 1 photograph; 3 diagrams.

RICHARD P. STORRS, M.D.
Los Angeles, Calif.

Unilateral Renal Damage After Translumbar Aortography. G. Pigeon, R. Lefebvre, G. E. Cartier, and J. Genest. Canad. M. A. J. **83:** 69–72, July 9, 1960. (Hôtel-Dieu Hospital, Montreal, Que., Canada)

The authors report a case of rapid renal atrophy following introduction, with a pressure injector apparatus, of 40 ml. of 70 per cent sodium acetrizoate directly into the right renal artery in the course of translumbar aortography. The patient was a 40-year-old man with recently discovered hypertension; he was unaware of a familial background of high blood pressure which subsequently came to light.

Cases of accidental direct injection of contrast medium into a renal artery, resulting in kidney injury, have been reported with volumes of 12 to 100 ml. of 70 per cent sodium acetrizoate. Such reports indicate the necessity of precautionary measures in undertaking translumbar aortography. The need for obtaining scout films during the intra-aortic injection of a few milliliters of radiopaque material to localize the tip of the needle is strongly stressed. Retrograde aortography by femoral artery catheterization also involves serious risks.

Sodium acetrizoate, although widely used, has definite nephrotoxic and neurotoxic properties. Less toxic radiopaque materials are 60 per cent Renografin and Vasurix 38.

Six illustrations.

Stenosis of the Right Main Pulmonary Artery. Clinical, Angiocardiographic, and Catheterization Findings in Ten Patients. Lawrence L. Luan, Joseph Lloyd D'Silva, Banjamin M. Gasul, and Robert F. Dillon. Circulation **21:** 1116–1125, June 1960. (Cook County Hospital, Chicago, Ill.)

The authors report 10 cases of isolated stenosis of the right main pulmonary artery, in all of which the diagnosis was confirmed by cardiac catheterization and dextro-angiocardiographic studies. The patients ranged in age from four months to thirteen years; 4 were boys and 6 were girls. Seven had associated cardiac anomalies.

No satisfactory etiologic explanation has been offered for the occurrence of stenosis of the right pulmonary artery. The fact that both absence of the pulmonary artery and its stenosis have been recorded more often on the right side suggests a common embryologic origin for those anomalies.

From their experience in these cases, the authors believe that the most common auscultatory finding is a systolic murmur of Grade II to IV intensity, heard over the second and third left or right intercostal spaces, depending on the location of the stenosis. This murmur usually radiates to the axillae and the interscapular region. Both the first and second heart sounds are essentially normal; this makes the differentiation from

the other acyanotic congenital cardiac lesions clinically possible, particularly if diminished pulmonary vascularity of one lung is demonstrated roentgenographically. The electrocardiogram of patients with stenosis has a normal pattern unless associated lesions are present. Roentgenograms of the chest may show decreased vascularity of the right lung as compared to the left. This observation, together with the systolic murmur and the normal electrocardiogram, should permit clinical diagnosis of the anomaly. Angiocardiography usually demonstrates the stenosis of the right main pulmonary artery. At times, the stenotic area may not be visualized because of overlapping of the right atrial appendage. Right heart catheterization in the isolated form of stenosis shows no alteration in hemodynamics except for a pressure gradient across the stenotic area. This was obtained in all of the authors' cases except 1 in which the catheter could not be advanced beyond the main pulmonary artery.

In an addendum 3 additional cases are mentioned in which a clinical diagnosis of isolated stenosis of the right main pulmonary artery was based on auscultatory and roentegn findings, and this diagnosis was subsequently confirmed by angiocardiography and cardiac catheterization.

Five roentgenograms; 2 phonocardiograms; 2 pressure pulse tracings.

ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Surgical Treatment of Renal Hypertension. George C. Morris, Jr., Michael E. De Bakey, Denton A. Cooley, and E. Stanley Crawford. Ann. Surg. **151**: 854–866, June 1960. (Baylor University College of Medicine, Houston, Texas)

Renovascular hypertension resulting from partial occlusion of one or both renal arteries appears to be more common than formerly realized. The authors report their observations in 32 hypertensive patients in whom renal artery reconstructive procedures were performed. The diagnosis of this form of hypertension is dependent upon precise aortography with good delineation of the renal arteries. The technic which the authors have found most satisfactory consists of translumbar injection of 25 c.c. of 70 per cent Urokon high in the upper abdominal aorta. Employing this particular method, they have performed over 1,400 aortographic examinations without death or serious complication.

Idiopathic hypertension arising in patients under the age of thirty-five years or over fifty-five has been considered an indication for aortography, but none of the authors' 32 patients was less than thirty-five, and most were in the fourth, fifth, and sixth decades. Disparity in size of the kidneys as demonstrated by excretory pyelography has also been considered an indication for aortography; in only a minority of the present series, however, was a significant inequality of kidney size apparent. Delayed or poor excretion on one side, however, was commonly noted in the presence of both unilateral and bilateral renal artery stenosis, and this is felt to be one of the important indications for aortography.

Fourteen of the 32 patients had bilateral stenosis of the renal arteries. Associated aorto-iliac arteriosclerotic lesions, for the most part occlusive in nature, were concomitantly corrected in 23 instances. Renal revascularization was accomplished by utilizing the bypass graft principle for 34 renal arteries and patch graft reconstruction in 6. Multiple aneurysms of 1 renal artery required resection and graft replacement, and in 1 patient an endarterectomy through the aorta was performed.

The results of surgery in these cases were most gratifying, with significant reduction in blood pressure in all 32 cases. Seventy-five per cent obtained prompt, and as yet permanent, return to normal blood pressure. Most of the patients had postoperative aortograms, and all of these showed a satisfactory appearance of the renal revascularization.

Twelve figures, including 15 roentgenograms; 5 tables.

MUSTAFA BALKIR, M.D.
Cleveland Metropolitan General Hospital

The Diagnosis and Treatment of Renal-Artery Stenosis. J. J. Brown, K. Owen, W. S. Peart, J. I. S. Robertson, and D. Sutton. Brit. M. J. **2**: 327–338, July 30, 1960. (St. Mary's Hospital, London, England)

Since 1957, the authors have performed renal arteriography routinely in patients with severe hypertension. Of 160 cases investigated in this way, a renal-artery lesion was demonstrated in 10; in 8 other cases renal-artery narrowing was revealed at aortography for other reasons. The present paper is based on a study of 22 patients in whom renal-artery disease was proved or strongly indicated.

Stenosis of the renal artery should be suspected particularly in the hypertensive patient with other manifestations of occlusive arterial disease. The most frequent cause is an atheromatous plaque, usually situated close to the origin of the artery. A systolic bruit arising in the stenosed artery is frequently heard, and occasionally a palpable thrill has been found in the affected vessel. The appearance of the ocular fundus varies with the phase of the disease. On ureteric catheterization studies the characteristic features of renal-artery stenosis are, on the side of the lesion, diminished urine flow; lowered clearances of inulin, creatine, and sodium para-amino-hippurate; and, usually, diminished urinary concentrations of sodium and chloride.

In many cases of renal-artery stenosis, plain radiographs have shown the affected kidney to be smaller than its counterpart, though not significantly so. In no patient was the unaffected kidney the smaller one. The concentration of contrast medium in the urine on the two sides parallels the inulin and creatinine concentrations. It is to be anticipated, therefore, that renal-artery stenosis will be represented on intravenous pyelography by higher contrast and better visualization on the affected side than on the normal, provided severe structural damage has not occurred in the kidney. Better contrast on the side with stenosis was, in fact, seen in 7 cases of the present series. When bilateral renal-artery stenosis exists, particularly good contrast may be expected on excretion urography.

For renal arteriography the authors prefer a modification of the percutaneous selective technic of Ödman (Acta radiol. **45**: 1, 1956. Abst. in Radiology **67**: 773, 1956). In one of the authors' cases a diagnosis of renal-artery stenosis was suggested incorrectly when the catheter tip virtually occluded the lumen of the artery supplying a small, irregular, and probably pyelonephritic kidney; further studies ruled out stenosis and it is presumed that the appearance was due to a jet effect as the contrast medium left the catheter tip. Unless a distinct pressure-drop across the site of supposed obstruction is found at operation, the diagnosis of a truly functional renal-artery stenosis should be

strongly questioned, whatever arteriography suggests.

In most patients with renal-artery stenosis, a reconstructive operation is desirable since the kidney distal to the stenosis is potentially the better of the two, being protected from hypertensive damage by the stenosis. Nephrectomy or reconstructive surgery was performed in 6 patients in the present series in whom a diagnosis of stenosis was established beyond reasonable doubt; in all but 1 there was a fall in the blood pressure to normal levels, with resolution of retinal abnormalities and a reduction in cardiac hypertrophy.

Fourteen figures, including 9 roentgenograms; 9 tables.

HANS A. LINDT, M.D.
Cleveland Metropolitan General Hospital

Renal Vascular Hypertension in Children. John P. Smith and Mark L. Saylor. J. Urol. **84:** 17–23, July 1960. (350 E. Broad St., Columbus 15, Ohio)

The cause of persistent hypertension in childhood may be a renal vascular lesion which can be corrected by surgery. Primary or essential hypertension occurs infrequently in children; its diagnosis and management remain within the province of the pediatrician. The authors here speak for the urologist, who is principally concerned with the renal conditions which lead to secondary hypertension, that is, renal parenchymal disease, renal vascular disease, and perinephritic disease. They discuss methods of evaluating the patient with suspected renal hypertension and present 3 illustrative cases.

A plain roentgenogram will give some indication as to the regularity of kidney outline or any disparity in renal size. Excretory pyelography is essential, but is not a reliable means of estimating renal function. Retrograde pyelography will further delineate any abnormality visualized on the excretory urogram. Individual renal function studies, such as phenolsulfonphthalein, indigo carmine, and urea clearance, can be obtained at this time. The determination of renal plasma flow will help to determine which is the "hypertensive" kidney. The presacral introduction of carbon dioxide into the retroperitoneum is helpful in outlining the kidney and suprarenal masses in children. Renal arteriography has its greatest application in the study of suspected renal vascular lesions. The authors prefer femoral selective catheter aortography. An open biopsy of both kidneys, by the transabdominal route, may be advisable to make certain that bilateral disease is not present.

The surgeon may elect to sacrifice a damaged kidney or repair the occlusive vascular anomaly. If children with renal hypertension are untreated, renal function will surely deteriorate. This fact justifies aggressive investigation and definitive surgical treatment.

Six roentgenograms; 1 photomicrograph; 1 drawing

WALTER EATON, JR., M.D.
University of Pennsylvania

Hypogastric Arteriography Prior to Continuous Infusion of Malignant Tumors of the Uterine Cervix and Vagina. Preliminary Report. Paul R. Zeit, C. Robert Hughes, John J. Cahill, and J. Gregory Hamilton. Cleveland Clin. Quart. **27:** 119–124, July 1960. (Cleveland Clinic, Cleveland 6, Ohio)

The study reported here was undertaken in connection with the treatment of a series of far-advanced tumors of the female pelvis by continuous intra-arterial infusion with amethopterin.

For maximum benefit from infusion of malignant tumors in any location, the following requirements must be met: (1) The one or two arteries selected for infusion must deliver most of their blood to the region of the tumor. (2) Most of the blood supply of the tumor itself must come from these arteries. (3) The vessels must be accessible and of adequate size to be catheterized easily. (4) Sacrifice of the artery utilized must be possible, if necessary, without damage to normal tissues. For infusion of carcinoma of the uterus, cervix, and upper vagina, the hypogastric artery fulfills these requirements.

The authors have performed arteriography in 9 cases in which hypogastric infusion was to be done. By this means they obtain information concerning the accuracy of placement of the catheter in the artery and an estimate of the amount of the drug that can be expected to reach the region of the pelvic tumor.

A hypogastric artery is exposed by reflecting the peritoneum. First the posterior trunk is ligated with a silk suture as close to its origin as possible in order to direct almost all of the hypogastric arterial blood flow into the organs of the pelvis. Two bulldog clamps are placed on the artery, one near its origin from the common iliac artery and the other well down on the anterior trunk. Between the two clamps a No. 18 needle is inserted through the wall of the vessel, and through the lumen of this needle a fine polyethylene catheter is threaded. The needle is withdrawn, the clamps are released, and 7 to 8 c.c. of Hypaque sodium 50 per cent is injected rapidly through the catheter. An anteroposterior film is exposed as the injection is completed. There have been no undesirable effects or complications arising from this procedure.

Three roentgenograms.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Differential Diagnosis of Benign and Malignant Tumors of the Extremity with the Aid of Angiography. L. Mucchi, G. L. Lorenzi, and I. F. Goidanich. Fortschr. a. d. Geb. d. Röntgenstrahlen **93:** 62–66, July 1960. (In German) (L. M., Via Chiossetto 14, Milan, Italy)

The authors studied angiographically a series of 162 cases of bone involvement, including specific and nonspecific inflammatory processes, traumatic changes, benign and malignant tumors. Of 56 bone tumors, 26 were benign and 30 malignant.

The angiograms in every case were obtained independently without the benefit of the history or clinical observation. The skeletal findings were not taken into consideration.

It was shown that angiographic changes of themselves make possible a differentiation between benign and malignant processes. In *benign tumors* the angiogram is normal. The characteristic angiographic findings in *malignant processes* are as follows: (1) at and around the tumor, a net of arteries of fluctuating caliber and irregular contour, the impression being that of newly formed vessels; (2) more or less regular passage of the contrast medium into the tumor, not only in the involved bone but periosteally, so that there is a generalized stain of the entire tumor area; (3) the presence of lacunas in the vessels of the tumor due to irregular collections of the contrast material; (4) direct passage of the contrast material from the arteries into the veins. The first radiograph outlines veins around the tumor.

The authors believe that angiography is the method of choice for differentiation between benign and malig-

nant tumors of the extremities and should be used routinely.

It may be possible that one day the pathognomonic angiogram for each bone disease will be established.

Eight roentgenograms. ILONA D. SCOTT, M.D.
Lewisburg, West Va.

Late Behavior of Vascular Substitutes: Three to Five Year Follow Up of Arterial Homografts and Synthetic Prostheses in Experimental Animals. John H. Foster, Carl-Axel Ekman, and H. William Scott, Jr. Ann. Surg. **151:** 867–878, June 1960. (Vanderbilt University School of Medicine, Nashville, Tenn.)

"Freeze-dry" ethylene oxide-sterilized aortic homografts and seamless nylon aortic prostheses were implanted in the abdominal aorta of 23 mongrel dogs and followed from three and one-half to five years. Aortography was done at least once yearly in each animal.

Although aortography and postmortem examination revealed degenerative changes in both types of grafts, from a clinical point of view the grafts functioned satisfactorily. Atherosclerotic deposits of lipids and calcium occurred in a significant percentage of both types of vascular substitutes. In 2 of 12 homografts, mild aneurysmal dilatation developed. Among 11 synthetic prostheses, mural thrombi were formed in 3 and intimal defects were found in 9.

The authors conclude that neither the freeze-dry ethylene oxide homograft nor the seamless nylon prosthesis is the ideal vascular substitute.

Twelve roentgenograms; 9 photomicrographs; 5 photographs; 2 tables. MUSTAFA BALKIR, M.D.
Cleveland Metropolitan General Hospital

THE DIGESTIVE SYSTEM

The Etiology and Management of the Dumping Syndrome Following a Gastroenterostomy or Subtotal Gastrectomy. William E. Abbott, H. Krieger, S. Levey, and J. Bradshaw. Gastroenterology **39:** 12–26, July 1960. (University Hospitals, Cleveland 6, Ohio)

A variety of postgastrectomy ills may result when the reservoir capacity of the stomach is lost by the creation of an artificial stoma which negates the function of the pylorus. The authors classify the abnormalities into eight broad categories: (1) recurrent ulceration and fistula; (2) improper anastomosis, with partial or complete obstruction of the stoma; (3) afferent loop malfunction; (4) anemia; (5) undernutriton; (6) hypoglycemia; (7) diarrhea; (8) dumping syndrome. The purpose of this paper is to elucidate the more important mechanisms and the pathophysiology of the dumping syndrome and to attempt to show that stomal size is of prime importance in influencing the rate of emptying of the gastric remnant after a gastroenterostomy with or without a partial gastrectomy.

The most important study in evaluating gastrointestinal function is a "functional" x-ray examination following ingestion of a mixture of barium and "blendzined" food. Seventy grams of barium were mixed in a blender with Protenum, milk, ice cream, and sugar, to obtain a chocolate-flavored drink, providing 19.5 gm. of protein, 11.3 gm. of fat, and 46 gm. of carbohydrate in a total volume of 330 c.c. The carbohydrate content was sufficiently high that it often induced symptoms in symptomatic "dumpers" or in patients with rapid gastric evacuation from whom no signs or symptoms could previously be elicited (latent symptomatic dumpers). The patient (fasted and ambulatory) ingested the barium-food mixture over a four-minute period, and upright 14 × 17-inch roentgenograms were taken after one, twenty, forty-five, and ninety minutes. Fluoroscopy and manipulation were not employed, and the patient stood or sat during the procedure.

In more than 20 normal adult volunteers who were examined in this manner, the barium mixture was discharged slowly from the stomach over a period of two hours or more, and the head of the column usually did not reach the cecum within two hours. Studies in symptomatic patients often revealed an almost complete lack of reservoir capacity of the stomach, with the barium in the terminal ileum in one minute and in the ascending colon in twenty minutes.

The authors feel that the only effective operation for peptic ulcer is one that preserves the reservoir capacity of the stomach. At present they believe this can be accomplished only by making a stoma with an internal diameter of 1 to 1.5 cm. They have converted a large gastrojejunostomy stoma to a small stoma in 15 patients with benefit in all cases and excellent results in most. Approximately 100 gastrectomized patients have been studied over the past seven years. In many of these, small stomas had been produced and in this group no dumpers were found. During the same period, most of the patients with large stomas proved to be dumpers. It is hoped that in the future operations will be utilized which prevent rapid gastric emptying.

The case histories and roentgenograms of 4 patients are included as typical examples of the undesirable sequelae of the functional or anatomical loss of the reservoir capacity of the stomach.

Twenty-four roentgenograms; 1 diagram.
RICHARD A. ELMER, M.D.
Atlanta, Ga.

Adenocarcinoma of the Stomach with Calcification. A Case Report. G. O. McGinnis. Gastroenterology **39:** 90–93, July 1960. (U. S. Army Hospital, Sandia Base, Albuquerque, N. Mex.)

A case of mucinous adenoma of the stomach with calcification is reported. The author was able to find only 5 similar cases in the English literature. His patient was a 34-year-old Negro. A plain film of the abdomen revealed stippled calcium deposits in the left upper quadrant; on a roentgenogram taken after the ingestion of barium these deposits were seen to lie chiefly along the lesser curvature of the stomach. A gastrointestinal series showed a poorly defined polypoid area of defective filling in the midportion of the lesser curvature. The mucosal pattern was irregular. Except for the calcification, the appearance did not differ from that of ordinary carcinoma of the stomach.

In this case and the other cases reviewed, pathologic examination showed the tumor to contain large amounts of mucin as well as the calcium deposits evident on the roentgenograms. The diffuse type of calcification seen in the present case is easily differentiated from calcium deposits in arteries, adrenal glands, lymph nodes, spleen, and benign gastric lesions. Diffuse calcification in the pancreas, however, could easily simulate calcification limited to the lower third of the stomach. Leiomyomas of the stomach rarely contain roentgenologically demonstrable calcium.

Two roentgenograms; 1 photomicrograph.
RICHARD A. ELMER, M.D.
Atlanta, Ga.

An Evaluation of the Einhorn String Test. J. A. Ewart, H. N. Sturtevant, and B. H. Sullivan, Jr. Am. J. Digest. Dis. **5:** 632–638, July 1960. (Lackland AFB, Texas)

Having observed a case in which repeated gastrointestinal series were negative but the Einhorn string test for ulcer was consistently positive, the authors undertook a critical evaluation of the latter procedure. Twenty-five test examinations were accomplished with strings prepared with radiopaque markers placed at 5-cm. intervals from the distal end. With the string in place, these markers were located in reference to the gastrointestinal tract radiographically. By comparison of the blood stain on the string in reference to the markers, the site of origin of the blood was determined. All of the patients had at least one x-ray examination; gastroscopy was performed when it was felt to be indicated, and in some instances the diagnosis was confirmed surgically.

The following conclusions were reached: (1) There is no positive correlation between the location of the blood stain on the string and the lesion in the gastrointestinal tract. (2) Localizing the lesion with reference to the distance of the blood stain from the incisor teeth or to the bile stain is quite unreliable. (3) The bile stain on the string was demonstrated to lie within the stomach in 50 per cent of the cases reviewed. (4) The string test is of no practical value in either the diagnosis or location of a peptic ulcer.

THEODORE E. KEATS, M.D.
University of Missouri

Adult Megacolon Without Obstruction. Myron Melamed, Anton M. Pantone, and Jack Williams. Illinois M. J. **118:** 31–32, July 1960. (College of Medicine, University of Illinois, Chicago, Ill.)

Two cases are reported in which extreme degrees of colon dilatation were not related to mechanical bowel obstruction. In 1 patient, a 75-year-old male, the distention was considered the result of an unusual form of paralytic ileus; in the other, a 68-year-old woman admitted to the hospital with a clinical diagnosis of cerebral vascular accident, the cause was thought to be a "neurologic disturbance."

The possibility of "functional" disorder producing abdominal distention with extreme degrees of megacolon should be kept in mind.

Five roentgenograms.

An Evaluation of the Hazards of Barium Enema Examination. Roger Pyle and Eric Samuel. Clin. Radiol. (J. Fac. Radiologists) **11:** 192–196, July 1960. (Royal Infirmary, Edinburgh, Scotland)

The authors discuss the potential complications inherent in the barium-enema examination and in the cleansing enema, and the precautions to be taken to avoid them.

Injury to the bowel wall from an incorrectly inserted enema tube is the most common complication. Perforation of the colon apart from direct trauma by the nozzle has also been reported. In this connection the authors warn against raising the fluid reservoir higher than 3 feet in order to obtain a more rapid flow. Another serious complication is "water intoxication." The occurrence of burns due to too warm an enema is also mentioned.

The specific complications of the barium enema are rare. Leakage of barium-enema fluid outside the bowel carries the same mortality as perforations following an ordinary enema. Barium granulomas have been reported as a sequela of leakage of barium. Intestinal obstruction due to the combination of barium sulfate and feces into hard masses occasionally occurs. Fatal barium sulfate embolus has been observed.

The double-contrast examination may result in perforation with retroperitoneal and mediastinal emphysema. A case illustrating this type of complication is reported.

Four roentgenograms.

THEODORE E. KEATS, M.D.
University of Missouri

Fatal Embolization of Pulmonary Capillaries. Report of Case Associated with Routine Barium Enema. Keith M. Truemner, Stanley White, and Homer Vanlandingham. J. A. M. A. **173:** 1089–1092, July 9, 1960. (2400 North Rockton Ave., Rockford, Ill.)

Fatal embolization by entry of barium sulfate into the venous circulation during administration of a barium enema has been previously reported (Roman, Wagner, and Steinbach: Radiology **59:** 190, 1952). The authors present a second case in which the mechanism of death was acute massive embolization of small pulmonary vessels.

A barium-enema study was to be done on a 76-year-old woman, complaining of constipation with the urge to defecate but no passage of stool. Rectovaginal examination indicated a nodular mass of doubtful nature in the cul-de-sac. Sigmoidoscopy revealed a firm constriction in the region of this mass, but the mucosal pattern was normal. A Bardex bag was inflated and injection of barium was begun, but the patient could not tolerate the procedure and it was terminated. She complained of pain and while at stool, just after the bag was removed, she suddenly died. A little fresh blood was noted on her clothing and about the anus.

The pertinent autopsy findings in this case were revealed by viewing histologic sections of the lung with reduced illumination. Most of the alveolar capillaries and many larger vessels contained crystalline bodies ranging from small amorphous granules to irregular refractile bodies measuring 10 to 12 micra. There was no gross evidence of trauma to the mucosa of the colon, sigmoid, rectum, or anus. Numerous diverticula were noted. Sections contained minor inflammatory foci about these structures but no fresh hemorrhage. A few dilated submucosal vessels, in the histologic sections, showed crystalline bodies. Hemorrhoidal varicosities were not grossly apparent.

The kidneys showed crystalline bodies in the glomerular capillaries, similar to those in the lung although smaller in size and number.

The authors conclude that the pathogenesis of this type of accident reflects the following three factors: (1) minor and perhaps unavoidable trauma to submucosal venous channels, either normal, or somewhat hemorrhoidal in character; (2) the "aspirating" ability of venous plexuses; and (3) the existence of increased luminal pressure within the distal segment of the colon. It is their belief that sublethal embolization is conceivable and that "reactions" which sometimes occur during barium-enema studies may not necessarily be emotional, cardiovascular, or reflex in character.

Three photomicrographs.

JOHN P. FOTOPOULOS, M.D.
Northwestern University Medical School

Retroperitoneal Emphysema as a Complication of Barium Enema. F. J. Brunton. Clin. Radiol. (J. Fac. Radiologists) **11:** 197–199, July 1960. (St. Mary's Hospital, London, W. 2, England)

A case of widespread interstitial retroperitoneal emphysema following air insufflation during a barium-enema examination in an elderly woman with diverticulitis is reported. Attention is called to 5 similar recorded incidents. In several instances the interstitial emphysema indicated probable rectal damage that might otherwise have passed unnoticed. The author warns that particular care is necessary in the performance of a barium-enema study in patients in the older age group.

Four roentgenograms. THEODORE E. KEATS, M.D.
University of Missouri

Chemical Demonstration of Contrast Medium Precipitate in Human Gall Bladders. Georg Theander and Sten Veige. Gastroenterology **39:** 74–75, July 1960. (Malmö Allmänna Sjukhus, Malmö, Sweden)

Iopanoic acid (Telepaque) and its sodium salt can produce a radiopaque precipitate in the gallbladder. Occasionally, the precipitate has been demonstrated roentgenologically. The authors have studied the incidence and nature of these precipitates by chemical analysis of the bile.

Six grams of Telepaque was administered to 10 patients the evening before roentgenography and subsequent surgery. A small amount of radiopaque precipitate was visualized on the cholecystogram of 1 of the patients. Samples for chemical analysis were obtained from this patient and 7 others. The cystic duct was ligated as soon as possible during surgery to prevent the escape of gallbladder contents. After excision of the gallbladders, concretions were removed with tweezers and the fluid content was diluted with distilled water and centrifuged. The sediment was thoroughly washed with distilled water and the sample was studied for iodine. The iodine content of the sediment ranged from 0.4 to 9.0 mg. in 7 gallbladders; in the patient with the roentgenologically demonstrable precipitate the iodine content was 56.0 mg.

The authors conclude that although the precipitate is seldom sufficient to permit roentgen visualization, it is frequently produced. RICHARD A. ELMER, M.D.
Atlanta, Ga.

Technique and Evaluation of Operative Cholangiography. James P. Isaacs and Marvin L. Daves. Surg., Gynec. & Obst. **111:** 103–112, July 1960. (The Johns Hopkins Hospital, Baltimore 5, Md.)

A consideration of the equipment, technic, and clinical value of operative cholangiography is presented. The results in 979 cases, the total experience in biliary tract surgery at the Johns Hopkins Hospital between January 1954 and January 1959, are summarized; in 157 of these cases, operative cholangiograms were obtained.

Cholangiography performed during routine cholecystectomy for gallstones in 87 patients revealed unsuspected stones in 7 (8.0 per cent) and congenital bile duct anomalies in 3 (3.4 per cent). Inadvertent milking of gallstones into the common duct during cholecystectomy was demonstrated by cholangiography in 3 cases.

Common duct explorations for stones were done without operative cholangiography in 150 patients with a positive yield of stones in 57 (38 per cent). Common duct explorations plus operative cholangiography yielded stones in 24 of 49 patients (49 per cent) and were negative in 25. Specifically, positive cholangiograms were confirmed by the finding of stones on exploration in 23 (95.8 per cent), while 24 negative cholangiograms (96 per cent), proved to be correct. Thus, the accuracy of operative cholangiography in the 49 cases was 96 per cent. Since the yield of stones from common duct exploration when cholangiography was performed was 11 per cent higher than when cholangiography was not undertaken, the procedure is recommended with all common duct explorations.

Hepatic duct stones were visualized by operative cholangiography in 6 of 49 patients having common duct explorations (10.5 per cent).

Cholangiography is contraindicated in patients with severe, acute inflammatory disease, when only minimal biliary dissection and exploration are advisable. In 153 cases of the present series, pyelograms were obtained twice. The significance of this finding is not known.

Thirty-five roentgenograms; 1 drawing; 1 table.
ROBERT JACOBS, M.D.
University of Pennsylvania

On Results Obtained with Tomographic Examination in the Study of the Bile Ducts with Intravenous Cholangiography. Clemente Crosta and Pier Alessandro Favero. Radiol. clin. **29:** 224–250, July 1960. (Istituto di patologia chirurgica dell'Università di Milano, Italy)

Because the routine examination of the bile ducts by intravenous cholangiography does not always achieve satisfactory results, the authors have used tomography routinely as a complementary method. They stress the following conclusions:

1. The tomographic examination of the bile ducts is simple and easy to perform. It gives precise results which make unnecessary repeated examinations.

2. Tomography, because of the precision of the results, is a necessary instrument of diagnosis in most cases. By the clarity of the pictures obtained, it has permitted the exclusion of any suspicion in normal cases and has been most helpful in pathological cases in which simple cholangiography afforded a doubtful or negative result.

3. The use of tomography facilitates the reading of simple cholangiograms.

4. When medication is used, tomography gives a better demonstration of the effects, showing at times interesting aspects invisible on the simple roentgenograms.

5. In cases in which surgery is indicated, tomography offers particular advantages, permitting the exclusion of lesions of the ducts, revealing the presence of unsuspected stones, confirming and localizing others, affording precise information as to the morphological and functional condition of the walls and the sphincter of Oddi.

The results obtained by the tomographic examination have permitted the surgeon to undertake intervention with a clearer vision of the condition of the biliary tract.

A table listing 71 cases, with the tomographic results, is included.

Forty roentgenograms (plain films and tomograms).
RENÉ HOURI, M.D.
New York, N. Y.

THE MUSCULOSKELETAL SYSTEM

Osteogenesis Imperfecta: Review of Literature with a Report on Three Cases. A. Awwaad and M. Reda. Arch. Pediat. **77**: 280–290, July 1960. (Faculty of Medicine, Ein Shams University, Cairo, Egypt)

A review of the literature on osteogenesis imperfecta is given, together with a report on 3 cases. Luck's classification (Bone and Joint Diseases. Springfield, Ill., Charles C Thomas, 1950) is briefly discussed: (1) *Osteogenesis congenitalis* or *fetalis* is the most severe form of the disease, the infant commonly being born dead or dying shortly after birth. (2) In *osteogenesis infantilis*, the infant is apparently normal at birth except for the possible occurrence of blue sclerae. Progress appears satisfactory until a fracture occurs as a result of a fall, perhaps as the child is learning to walk or to take a few steps; the intensity of involvement varies greatly. (3) In *osteogenesis tarda* there is sometimes substantial ossification of the skeleton at birth, with fractures and deformities occurring during late childhood (end of fifth year or later). The outlook as regards life is good, although the deformities frequently interfere greatly with activities and the patient usually ends up a miserably deformed dwarf. (4) *Osteogenesis adulta* is exceedingly rare, with recurrence of skeletal fragility developing in adult life after an apparent arrest of the infantile or tarda type.

Of the 3 cases reported, Case I was a typical example of the congenital type of the disease, while Cases II and III, in sisters, were of osteogenesis infantilis and tarda, respectively.

Roentgen examination in a 50-day-old girl, (Case I) showed partial ossification in some parts of the occipital, parietal, and frontal bones; irregular broadening of the ribs at sites of fractures and callus formation; broadening of the long bones with a generalized decalcification and crumpled-up appearance due to numerous fractures with ample callus formation. The patient remained in the hospital four weeks and died three months following discharge, of intercurrent bronchopneumonia, after sustaining more fractures of the limbs and ribs.

The mother of the patients in Cases II and III had had 6 abortions and given birth to 7 full-term, apparently normal infants, of whom 4 died. One of the 4 was reported to have had "the picture of osteogenesis imperfecta." Roentgenograms in Case II demonstrated platybasia, prominence of the jaws, multiple deformities of the spine, chest, bony pelvis, and long bones. During a four-year follow-up, the fractures became less frequent, but the patient was a crippled dwarf at sixteen years. Menses had not started and there was no growth of pubic or axillary hair.

The younger sister (Case III) was six years old when first admitted to the hospital. Roentgenographically, there was generalized and marked rarefaction of the ribs and vertebral bodies, with severe deformity of the chest cage but no evidence of old or recent fractures. Kyphoscoliosis was marked in the dorsal and upper lumbar regions. The long bones were normal except for several horizontal lines of arrested growth at the lower ends of both tibias. During the four years after the patient was first seen, she sustained no more fractures and at the time of this report was attending school regularly.

Six roentgenograms; 3 photographs.

The Radiological Diagnosis of Osteoporosis: A New Approach. Ellis Barnett and B. E. C. Nordin. Clin. Radiol. (J. Fac. Radiologists) **11**: 166–174, July 196 (Western Infirmary, Glasgow, Scotland)

The authors describe a new procedure for the radiologic assessment of osteoporosis which they feel may prove useful in the routine screening of suspected cases until a satisfactory method of measuring vertebral body density can be evolved. Their approach depends upon the determination of cortex to shaft ratio in a femur and a metacarpal and the measurement of biconcavity in the spine. Arbitrary normal standards have been established in a control series of 125 adult outpatients. When the procedure was applied to about 150 persons suspected of having metabolic bone disease, abnormal results were obtained in 87 (71 women and 16 men).

The validity of the method depends in the final analysis upon the relationship between the x-ray score and other means of assessing osteoporosis, particularly bone biopsy. When judged by this criterion, the x-ray score bears a reasonable relationship to the histology of the iliac bone in the cases in which this comparison has been made so far.

The authors' scoring procedures suggest for the first time that there may be two types of osteoporosis—spinal and peripheral.

Twenty figures, including 9 roentgenograms; 2 tables.

THEODORE E. KEATS, M.D.
University of Missouri

Environmental Bone Disease of Hitherto Undescribed Type. N. F. Dodd, D. W. Levy, and W. P. U. Jackson. South African M. J. **34**: 606–611, July 16, 1960. (Groote Schuur Hospital, Cape Town, Union of South Africa)

This article is a preliminary report of an unusual bone disorder, closely related to fluorosis, which occurs in a small community in the northeastern Karroo in Cape Province, Union of South Africa. The condition begins with complaints of pain in the legs in children three to five years old; bone deformities, consisting mainly of bowing of the femora and tibiae, are manifested between the ages of five and six.

Two cases are reported: in a 13-year-old girl (Case I) and a 15-year-old boy (Case II). In each the bone and chronological ages were compatible. Roentgenograms in Case I showed evidence of generalized coarsening of trabeculae with demineralization and thinning of cortices. There was thickening of the outer table of the skull. The teeth had a defective lamina dura of the upper incisors, areas of erosion in some of the crowns, and tapering of the central incisors toward the apices in a peculiar fashion. The vertebral bodies were somewhat flattened and porotic, showing double transverse lines in each body. The femora were bowed laterally with thinning of the cortex and buttressing on the convex aspect. In Case II, radiographs demonstrated rather indefinite outlines in some of the bones, cortical thickening of the long bones, and apparent generalized sclerosis as seen in moderately advanced fluorosis, with coarse trabecular pattern and early calcification at the attachments of the ligaments and muscles. The femora and tibiae were bowed, as in Case I.

The roentgenograms of the pelvis and upper ends of the femora of both parents of the second patient were obtained. There was gross generalized sclerosis, with obliteration of the trabecular pattern and thickening of

the cortices of the femora. Irregular outlines of the bones were produced by calcification in several ligamentous and muscular attachments.

Classically, fluorosis manifests radiologically as a marked sclerosis, at first with accentuation of the trabecular structure. Later, apparent coalescence of trabeculae gives a picture of generalized uniformly increased density of bones, which appear hazy in outline, chalky, and structureless. The regions of the spine and pelvis are most affected. In advanced cases calcification of the ligaments can occur. The end stage is that seen in the pelves of the 2 adults described in the preceding paragraph. Case II could be said to show a roentgen picture somewhere between that of Case I and the one of his parents.

Taking all the unusual aspects of their cases into account, the authors postulate that fluorine is only one of the factors of the disease, though probably the most important, and that, in combination with either some other deficiency or a secondary factor yet unknown, fluorosis is occurring in an enhanced, accelerated, and unusual form.

Eight roentgenograms; 7 photographs; 1 diagram.

Chondrodystrophia Congenita Punctata (Conradi's Disease). Review of Literature and Report of Case with Unusual Features. Mathea Allansmith and Edward Senz. J. Dis. Child. **100:** 109–116, July 1960. (University of California Medical Center, San Francisco 22, Calif.)

A case of Conradi's disease (chondrodystrophia congenita punctata) is reported and the findings in 54 previously recorded cases are tabulated. This rare disorder of the bones of the fetus and newborn is characterized roentgenographically by multiple minute and usually discrete areas of calcification, resembling splattered paint, in the epiphyses, which are enlarged and deformed, with a mushroom-like appearance. These "paint-splattered" spots may be visualized earlier than the date at which ossification normally begins. Over the first two or three years of life the deposits seem to regress.

Contractures were reported in 25 of the 55 cases of Conradi's disease, proximal shortening of the limbs in 27, and dwarfing in stature in 26. In the remaining cases these features were not mentioned or were not present. In 17 of the cases there were bilateral cataracts. The presence of cataracts is of great diagnostic and prognostic value, ruling out the milder congenital anomalies of bone growth that usually carry a good prognosis, such as fetal chondrodystrophy, dysplasia epiphysalis multiplex, and stippled epiphyses of the acquired variety. The skin was abnormal in 13 cases, normal in 7, and its condition was not mentioned in 35.

There is strong evidence that Conradi's disease is familial; of 48 families studied, 5 had 2 or more children with the disease. A common abnormality—flattening of bridge of the nose—was found in 21 cases. Four children had heart abnormalities and 7 had a high palate. Seventeen (30 per cent) died in the first year of life.

The authors' patient was followed for four and one-half years; at that time she was dwarfed but mentally alert.

Two roentgenograms; 2 photographs; 1 table.

DONALD F. LOEFFLER, M.D.
University Hospitals, Cleveland, Ohio

Salmonella Osteitis in Nigerian Children. R. G. Hendrickse and Patrick Collard. Lancet **1:** 80–82, Jan. 9, 1960. (University College, Ibadan, Nigeria)

The authors report 13 cases of *Salmonella* osteitis seen in the University College Hospital of Ibadan, Nigeria, between June 1956 and October 1958. In 7 cases the salmonellal infection complicated sickle-cell anemia; in 1 case sickling was not present, and in 5 it was not looked for. These cases showed a definite peak incidence during the months of June, July, and August, when the rainy season is at its height. Eight different strains of *Salmonella* were isolated. Nine of the 13 patients were under two years of age.

Multiple sites of osteitis were visualized roentgenographically in all cases, and in some the lesions were bilateral and symmetrical. The finding of 7 examples of *Salmonella* osteitis in proved cases of sickle-cell anemia supports the observation that persons with sickle-cell anemia are peculiarly susceptible to this complication. Readers interested in this subject are referred to the article by Wigh and Thompson (Radiology **55:** 553, 1950) and the comment upon it by Drs. Hodges and Holt in the 1951 *Year Book of Radiology*, p. 88.

Seven roentgenograms; 2 tables.

Roentgen Diagnosis of Destructive Syphilis of the Spine. M. Sgalitzer. Wien. klin. Wchnschr. **72:** 714–719, Oct. 14, 1960 (In German) (1623 Brennen Road, Columbia, S. C.)

Destructive syphilis of the spine, which is of rare occurrence, is due to direct invasion by spirochetes, whereas in the tabetic or Charcot spine the causative organism invades the central nervous system. The site of predilection is the cervical area, but occasionally the dorsolumbar spine is involved.

Characteristic roentgenologic features are a moth-eaten appearance of the vertebral bodies, erosion anteriorly with an irregularly serrate contour of the upper plate, and sclerotic change with hyperostosis and massive osseous bridging. The ligaments are frequently ossified, but the disks remain intact. There is no paravertebral abscess, very little deviation of the vertebral axis, and but little flattening of the bodies in spite of marked destruction of bone. The sclerotic bone apparently supplies the necessary support.

The roentgenologic findings are rather specific, but somewhat puzzling at first, especially when only a single vertebra in the dorsolumbar area is involved. A subsequent survey of the skeleton may reveal characteristic bone lesions elsewhere, and when serologic tests for syphilis prove positive, a correct diagnosis of the vertebral lesion can be established.

Seven cases are reported, 5 of which are illustrated. The series includes 2 cases previously recorded (Radiology **37:** 75, 1941). The cervical spine was involved in 5 and the lumbar spine in 2. One of the patients had also lesions in the skull, both humeri, and the pelvis. In another patient a humerus was involved in addition to the cervical spine.

Localized symptoms were severe in some and mild in others. In 3 cases the correct diagnosis was first suggested by the roentgenologist and later confirmed clinically. Antisyphilitic therapy brought about relief in all patients. One of these had suffered agonizing pain for twenty years, which could not be alleviated by any kind of nonspecific therapy.

In the differential diagnosis the following conditions are to be considered: osteomyelitis, lymphogranulomatosis, leukemia, primary sarcoma, and metastatic malignant lesions.

Five roentgenograms. ERNEST KRAFT, M.D.
Northport, N. Y.

Actinomycosis with Involvement of the Vertebral Column: Case Report and Review of the Literature. W. B. Young. Clin. Radiol. (J. Fac. Radiologists) **11:** 175–182, July 1960. (Royal Free Hospital, London, England)

The author reports a case of actinomycosis of the lung with secondary involvement of the spine. The patient was a 42-year-old man who complained of persistent pain in the left chest which was aggravated by coughing or taking a deep breath, stiffness of the neck, and a lump in the side of the neck. Five months previously he had been seen because of an irritant cough and an abscess on the chest wall overlying the left tenth rib. At that time radiographs revealed an ill defined density at the left lung base with linear streaks directed toward the hilus. The left costophrenic angle was obliterated by pleural effusion, and the left tenth rib appeared thinned and showed a single layer of periosteal new bone. Over this there was a localized swelling of the soft tissues. The abscess on the chest wall was incised; the wound healed quickly, and the cough disappeared. On the patient's second admission, radiographs showed a broad, well demarcated homogeneous shadow in the superior mediastinum with displacement of the trachea to the right. There was general decalcification and scattered bone destruction of the bodies and transverse processes of the upper thoracic and lower cervical vertebrae and of the posterior parts of the upper five ribs. On lateral films of the chest and neck the soft-tissue density was seen to lie mainly in the posterior and superior mediastinum but passed forward and then downward along the back of the manubrium as far as the manubriosternal junction. It extended up into the prevertebral tissues of the neck, displacing the esophagus and trachea forward. The swelling in the left posterior triangle was incised, and a small amount of purulent fluid was released. Examination of tissue taken for biopsy revealed *Actinomycosis bovis*. On penicillin therapy the patient's condition improved, and the last radiographs reported showed that the affected vertebrae had returned to normal and the paravertebral phlegmon had been absorbed.

Actinomycosis of the spine in most cases occurs as a result of direct extension of a nearby focus of infection, almost invariably in the form of a paravertebral phlegmon. There is a tendency for several successive vertebrae to be affected, though not always to the same degree. None of the component parts of a vertebra are immune from attack, although the transverse processes and body are usually invaded before the pedicles, laminae, and spinous processes. In disease of the thoracic spine, the posterior ends of the corresponding ribs are almost always involved.

The earliest lesions are surface erosions, which on the lateral film give the anterior profiles of the affected bodies a ragged or saw-toothed appearance. The underlying cancellous bone is then attacked and destroyed, producing ill defined patchy areas of destruction in the vertebral bodies.

New bone is laid down around the foci of destruction. Usually the destructive process advances slowly, so that the affected part of the skeleton is excavated and burrowed, with the formation of channels of suppuration bounded by bone of varying thickness and density. In acute cases osteoclasis and destruction give the affected bones a decayed, moth-eaten and porotic appearance. In most chronic cases, defensive forces keep pace with, or outstrip, those of destruction, and new bone is deposited around the abscess pockets producing a coarse honeycomb or lattice appearance. Sometimes new bone appears to be formed in excess, so that the bone is increased in girth and bony bridges span adjacent vertebrae or transverse processes and ribs. Whichever type predominates, the formation of sequestra, as seen in pyogenic osteomyelitis, does not seem to occur. There is almost always evidence of reactionary subperiosteal new bone, though it tends to be inconspicuous.

Veretebral collapse is said to be uncommon. The intervertebral disks are relatively immune and, if invaded, appear to suffer only minimal destruction. There is nearly always radiological evidence of a paravertebral phlegmon, but this never contains calcium or opaque debris. There may be radiological evidence of pulmonary involvement, ranging from a localized area of consolidation to large areas of suppuration and fibrosis, commonly situated posteriorly, and not infrequently basal. In the cervical region the phlegmon can be recognized on the lateral film as an increase in depth of the prevertebral soft-tissue shadow and there may be evidence of disease of the mandible. It has been stated that involvement of the ribs and sternum in association with parenchymal infiltration and pleural thickening is more likely due to actinomycosis than any other condition (Kirklin and Hefke: Am. J. Surg. **13:** 1, 1931). If certain other chronic forms of empyema are excluded, this is possibly true.

Radiologic differential diagnosis includes tuberculosis, osteomyelitis, and metastatic carcinoma of the lung, secondary malignant involvement of the spine; syphilitic vertebral osteitis; and blastomycosis. Blastomycosis may present a picture almost identical and indistinguishable from that of actinomycosis and can be differentiated only by isolation of the organism or by fixation or hypersensitivity tests.

Eight roentgenograms; 1 photomicrograph.

THEODORE E. KEATS, M.D.
University of Missouri

Dysphagia and Hypertrophic Spurring of the Cervical Spine. David A. Hilding and Mihran O. Tachdjian. New England J. Med. **263:** 11–14, July 7, 1960. (Ireland Army Hospital, Ft. Knox, Ky.)

If the usually asymptomatic anterior hypertrophic spur of the cervical vertebra projects into the pharynx enough to impinge upon the food passageway, it can mechanically interfere with deglutition. Pain or difficulty in swallowing, foreign-body sensation, lump in the throat, and a constant urge to clear the throat are symptoms attributed to this condition. The authors add to the literature 3 cases of dysphagia caused by hypertrophic spurring of the cervical spine, 1 of which was successfully treated by excision of the osteophyte. One of the patients was a six-year-old boy in whom a developmental abnormality of the cervical spine at the C2-C3 level had resulted in a bony mass projecting into the pharynx.

Of the 36 previously reported cases, 22 were in males with a mean age of 60.8 years and a range from thirty-

nine to eighty years. In 22 patients one pair of vertebrae was involved. The junction of the fifth and sixth cervical vertebrae was involved in 41 per cent, that of the fourth and fifth in 23 per cent, and that of the second and third or third and fourth in 14 per cent each. When more than one pair was involved, the most common location of the osteophytosis was the third to fourth and the fourth to fifth cervical vertebrae.

The mass may often be visualized on routine examination with a tongue depressor or mirror. If it is low endoscopy may be necessary. Palpation shows a hard, smoothly rounded, nonmovable mass projecting into the pharynx from behind. Roentgen examination reveals a marked spurring of the anterior edges of the vertebral bodies, with formation of a mass projecting into the pharynx. Often the two bodies appeared to be joined by a bridge of bone.

Trauma is sometimes considered a factor in the etiology of this condition, but in only 4 of the cases reviewed was a history of any significant injury obtained. In most of the cases there seemed to be a gradual progression of symptoms. In 4 patients the dysphagia was severe enough to cause loss of weight. Peroral endoscopy is hazardous in patients with cervical hypertrophic spurring, and pre-endoscopic roentgenograms are indicated to rule out this condition.

Patients with dysphagia should be carefully examined for osteophytes of the cervical spine. Their presence, however, does not necessarily mean that they are the cause of the dysphagia, and careful evaluation is required to establish a cause-and-effect relation. Excision of the osteophyte is indicated if symptoms are severe enough to warrant such a major procedure. It has been performed in 4 of the reported cases.

Four roentgenograms.

JOHN P. FOTOPOULOS, M.D.
Northwestern University Medical School

Fracture of the Carpal Navicular. Diagnosis, Nonoperative Treatment, and Operative Treatment. Otto Russe. J. Bone & Joint Surg. **42-A:** 759–768, July 1960. (Kundratstrasse 37, Vienna, Austria)

The author discusses the problem of fracture of the carpal navicular. Its diagnosis is important since poor treatment or no treatment leads to non-union and may cause a painful and seriously disabled wrist. Early diagnosis and adequate treatment, however, yield full recovery in almost 100 per cent of the patients.

In cases in which a fracture of the carpal navicular is suspected, the author routinely takes the following roentgenograms: (1) a dorsovolar view, with the forearm in neutral position midway between pronation and supination and the wrist in slight dorsiflexion with the fingers closed into a fist; (2) a similar view, with the forearm in 15 to 20° of supination; (3) a true lateral view with the forearm in 90° of supination; (4) a dorsovolar view, with the forearm in 15 to 20° of pronation. Ulnar deviation of the wrist while these roentgenograms are made should not exceed 10° with fresh fractures to avoid distraction of the fragments. These four roentgenograms are made on one film, 18 x 24 cm. (with the use of a lead shield). Only in exceptional cases is it necessary to have further oblique views in 80, 70, 60, and 50° of supination or in 40° of pronation.

In the presence of pain without definite roentgenographic findings, even when the film is studied with a magnifying glass, the recommended procedure is application of a cast for two weeks followed by repetition of the roentgenograms. Should tenderness on pressure or pain on movement persist, even to a slight degree, the wrist should again be immobilized, and the roentgenograms repeated after another two weeks. Fissure fractures of the navicular occur that can be demonstrated only after three to four weeks, when absorption has widened the fracture cleft.

Approximately 70 per cent of navicular fractures are located in the middle third, 20 per cent in the proximal third, and 10 per cent in the distal third of the bone. The average time necessary for bony union to occur is longer for fractures in the proximal third—ten or twelve weeks—than for most fractures in the distal and middle thirds for which six to eight weeks immobilization is required.

Immobilization in fractures of the navicular should be continued until the roentgenograms show definite signs of bony union. In the absence of clearly visible osseous trabeculations bridging the fracture defect, one should look for increased density of the bone at the site of the former fracture cleft or on each side of the cleft. It is not generally known that these calcified bands in the fracture site, or on both sides of it, are signs of bone union in fresh fractures of the navicular. Such calcifications occur in about 40 per cent of recent fractures. In old fractures, of course, these bands cannot be considered as signs of bony union.

The author discusses the conservative and operative treatment of carpal-navicular fractures. This section of the article should be read in detail by those interested in that phase of the subject.

Sixteen roentgenograms; 23 photographs; 4 tables.

THEODORE E. KEATS, M.D.
University of Missouri

GYNECOLOGY AND OBSTETRICS

Radiologic Pelvimetry. Ulf Borell and Ingemar Fernström. Acta radiol. Suppl. 191, 1960. (Karolinska Sjukhuset, Stockholm, Sweden)

The authors present an impressive volume of case material from the Department of Women's Diseases of the Karolinska Sjukhuset (Stockholm), reporting on a series of 3,223 pelvimetries during the years 1940–57. All cases with large pelvic diameters and others in which adequate information was unavailable were excluded, leaving 381 cases for analysis. Of this group of patients, 18 had contraction of the pelvic inlet and 16 of the lower part of the pelvis. The association of contraction of the inlet and the distal pelvis was exceptional in this series, occurring in only 2 instances. The methods of measurement are listed, and a procedure for comparing the diagnostic value of the various pelvic diameters is explained. The distal part of the bony pelvis is defined as a zone between and including the mid plane and the outlet.

An account of a new pelvimetric technic is given. Three roentgen films are obtained at a tube-film distance of 90 cm.: (1) anteroposterior view of pelvic inlet with patient semirecumbent; (2) lateral view of pelvis, with a metal scale in the vulva; (3) view of the pubic arch, Chassard-Lapiné view, with coning over the pubic arch area. The lateral view is obtained first. If the sagittal diameter of the inlet is 11 cm. or more, the probability is that there is no inlet contraction; with measurements of 10.0 to 11.0 cm., disproportion is rare and probably due to head size; with 9.5 cm., contraction is frequent.

If the sum of the sagittal diameter between the lower border of the symphysis and the sacral tip, also obtained from the lateral view, and the posterior intertuberous diameter on the Chassard-Lapiné view is greater than 25 cm., the risk of contraction is minimal. If this sum is less than 25 cm., an interspinous measurement is added; the sum of the three measurements should be greater than 34 cm. to be negative for contraction. If the total is less than 32 cm., pelvic contraction is present.

The authors indicate two primary indications for radiologic pelvimetry: (1) a history of protracted labor in a previous pregnancy, probably due to small pelvic dimensions, and (2) arrest of the fetal head despite strong uterine contractions. An additional point of interest is the observation that a common sign of disproportion was disalignment of fetal parietals at the sagittal suture; a measurement of 4 mm. is considered normal.

This monograph deserves careful reading by anyone interested in pelvimetry with minimum exposure both to fetus and the maternal gonads. The flexibility of the method is considered to be advantageous.

Forty-nine figures; 10 tables.

JOHN E. RHODENBAUGH, M.D.
The Henry Ford Hospital

Unequivocal Radiological Evidence of Intra-Uterine Foetal Death, Including Demonstration of Gas Formation within the Foetal Circulation: Report of a Case, and Review of Thirty-Seven Cases of Foetal Death. Robert Bennett. Clin. Radiol. (J. Fac. Radiologists) 11: 200–204, July 1960. (King Edward Memorial Hospital for Women, Perth, Australia)

Radiological signs contributing to the diagnosis of fetal death are discussed. In more recent years, two useful signs have been recognized, each of which may provide early and irrefutable evidence of death of the fetus. These are: (1) evidence of fetal intravascular gas and (2) Deuel's halo sign. The latter is due to an increase in the width of the soft tissues between the radiolucent subcutaneous fat of the scalp and the bones of the fetal cranial vault. A case is reported in which these two signs were demonstrated.

The occurrence of fetal intravascular gas formation is undoubtedly much more frequent than the total number of recorded cases (70) would indicate. A review of the roentgenograms of 36 patients who underwent prepartum x-ray examination showed evidence of fetal intravascular gas formation in 5. The characteristic appearances that may be produced by the gas and some of the difficulties of interpretation are discussed.

This review also showed that Spalding's sign (overriding of skull bones with cephalic asymmetry) and evidence of lack of fetal tone were the most consistently helpful radiological signs in arriving at a diagnosis of fetal death. These signs were present in 26 and 18 cases of the present series respectively.

In no case in the series was there evidence of gas without other signs of maceration. As has been shown by other writers, however, it is when this sign is present alone that it becomes most valuable. It will certainly permit a more confident diagnosis to be made when other, perhaps less conclusive, signs of maceration are present.

Three roentgenograms; 3 diagrams; 1 table.

THEODORE E. KEATS, M.D.
University of Missouri

THE GENITOURINARY SYSTEM

Absence of Vesicoureteral Reflux in Normal Adult Males. Guy W. Leadbetter, Jr., James H. Duxbury, and Jack R. Dreyfuss. J. Urol. 84: 69–70, July 1960. (Massachusetts General Hospital, Boston 14, Mass.)

Because of the lack of information concerning the presence or absence of vesicoureteral reflux in normal adults, the authors carried out cystographic studies on 50 normal males. None of the men had any history or clinical evidence of urinary tract disease. If there was no residual urine on catheterization, 200 c.c. of 12 per cent sodium iodide and 30 c.c. of 70 per cent sodium acetrizoate (Urokon) were mixed and instilled into the urinary bladder. Delayed (fifteen to thirty minutes) and voiding films were obtained. Vesicoureteral reflux was not demonstrated in any subject.

From the results of this study and those of investigations by others in children, the authors conclude that vesicoureteral reflux is abnormal at all ages and that it is caused either by a primary congenital defect in the anatomic or physiologic relationship at the vesicoureteral junction or is secondary to obstruction, infection, or a neurogenic deficit of the lower urinary tract. In the patient with vesicoureteral reflux associated urinary tract abnormalities should be searched for and corrective therapy should be instituted if possible.

In an addendum to the paper, the authors state that they have been using cineradiographic technics in evaluating patients suspected of having vesicoureteral reflux. These studies indicate that in some instances cineradiography is the sole means of demonstrating reflux, since it may occur in a fleeting moment and may be easily missed by standard radiographic procedures.

ROBERT A. BEAROR, M.D.
University of Pennsylvania

Renal Papillary Necrosis. A Roentgenographic Study of 155 Cases. Nils Lindvall. Acta radiol. Suppl. 192, 1960. (Karolinska Sjukhuset, Stockholm, Sweden)

An abstract cannot do justice to this excellent study of 155 cases of renal papillary necrosis. The patients ranged in age from nineteen to seventy-one years; 131 were women and 24 men. All, with a single exception, had at some time during the period of roentgen observation showed the cavities which are typical of the condition. In the remaining patient, characteristic concretions were demonstrated.

Nineteen patients had diabetes mellitus and 3 chronic urinary obstruction; 85 gave a history indicating abuse of phenacetin preparations. The record in 12 cases referred specifically to the absence of diabetes, urinary obstruction, headache, and phenacetin abuse. In the remaining 35 cases there was no mention of phenacetin.

Intravenous urography was found to be adequate for diagnosis and detailed study in the great majority of the cases. The author believes that retrograde studies should be used only in those rare instances in which the intravenous method fails to give an adequate picture because of a permanent and severe reduction in kidney function.

Early changes, preceding cavity formation, are the result of necrosis of the papillae and beginning detachment. These findings include a local impairment of function, dilatation of the calyceal fornix, irregularity and blurring of the papillary contour, and off-shoots of contrast media from the calyx into the parenchyma.

The cavities formed are divided into two groups. In the medullary type, necrosis starts in the central portion of the papilla and, when detachment has taken place, the cavity formed communicates *via* the papillary tip with the calyx. Roentgen examination shows a contrast-filled cavity in the tip of the papilla, separated from the intact fornix by a thin parenchymal layer. In the papillary form, the whole papilla is necrotic, and frequently adjacent portions of the pyramid as well. Here detachment starts from the calyceal fornix and a cavity forms which constitutes a direct continuation of the calyx; thus no remaining fornix can be observed. As long as a detached papilla remains in the cavity, roentgen examination shows a so-called ring shadow, since the sloughed tissue produces a contrast defect in the cavity.

There is probably no fundamental difference between the two types of cavity since, in one-third of 254 kidneys in which this point could be evaluated roentgenographically, both were shown to be present. It was further noted that, with enlargement of the medullary cavities, they assumed a papillary appearance.

Typical concretions of papillary necrosis are composed of a calcareous shell surrounding a more or less radiolucent nucleus. They were noted in 41 kidneys. *B. proteus* infection in the presence of a crystallization nucleus in the form of the detached papillary tissue accounts for this high incidence.

One hundred and fifty-two kidneys were studied for change in size: 116 became smaller and 36 remained of normal size throughout the period of study.

There was no direct correlation between the number of papillae destroyed and kidney function; however, there was a clear relationship between kidney size and urographic function. Both size and function appear to depend upon the coexisting pyelonephritis, which is consequently, in most cases, decisive as to prognosis.

Differential diagnosis is discussed, with respect to renal tuberculosis, renal dysplasia, calyceal cyst, medullary sponge kidney, pyelonephritis without papillary necrosis, hydronephrosis, tumor of the renal pelvis, and parenchymal reflux on pelography.

The roentgen and histologic findings agree closely in regard to both the distribution and the duration of the necrosis; however, a close correlation cannot be demonstrated between the roentgen changes and different combinations of clinical features.

The increased incidence of renal papillary necrosis during the past few years must be attributed partly to widened knowledge of the disease, partly to present-day possibilities of making the diagnosis during life, and probably partly to a true rise in frequency, with phenacetin abuse playing a role. It is noted that there is much to suggest that the papillary necrosis is caused by pyelonephritis instead of the reverse, and it is thus to be regarded as a symptom and not as a disease entity.

Fifty-eight figures; 7 tables.

MAX D. CLARK, M.D.
The Henry Ford Hospital

Association of Calyceal Diverticulum and Butterfly Vertebra. A. Schwartz, A. Pfau, and H. Weinberg. J. Urol. **84:** 32–35, July 1960. (Hadassah University Hospital, Jerusalem, Israel)

A calyceal diverticulum has been defined as "a urine-containing cavity situated peripheral to a calyx and connected to it by a narrow channel." The lining is identical with that of the pelvis and calyces. In uncomplicated cases, the surrounding renal parenchyma is normal. Some authors believe that these cavities are developmental anomalies, others consider them to be acquired.

Two cases are reported in which a calyceal diverticulum was associated with a butterfly vertebra, in one case of T-7, and in the other of T-11. One case was complicated by infection and stones, whereas the other was without urologic symptoms.

It is well known that developmental anomalies of the lumbosacral spine and of the genitourinary tract are often associated. However, no mention was found in the literature of the coexistence of a spinal anomaly with calyceal diverticula. The occurrence of these two rare abnormalities in the same person is unlikely to be purely a matter of chance.

The butterfly vertebra is due to failure of the two lateral halves of the cartilaginous vertebral body to fuse. As the calyceal diverticulum has the same lining as the calyx, it probably arises from the ureteric bud. Both chondrification of the vertebral body and development of the ureteric bud from the mesonephric duct occur at the same stage in the embryo, at about thirty-five days. It is therefore conceivable that a damaging influence acting upon the embryo at this stage might well produce disturbed development of the vertebrae and of derivatives of the ureteric bud, resulting in the deformities described here. The association of the two conditions lends support to the opinion that calyceal diverticulum is a developmental anomaly. Search for anomalies of the spine in patients with calyceal diverticula and *vice versa* may contribute further to the elucidation of the nature of this relationship.

Five roentgenograms.

IRVING J. WEIGENSBERG, M.D.
University of Pennsylvania

A Pyelographic Study of Ureteric Injuries Sustained During Hysterectomy for Benign Conditions. Edward Solomons, Emanuel J. Levin, Judah Bauman, and Joel Baron. Surg., Gynec. & Obst. **111:** 41–48, July 1960. (Maimonides Hospital, Brooklyn, N. Y.)

Because of its close proximity to the uterine artery, the cervix, and the lateral aspect of the vagina, the pelvic portion of the ureter is highly vulnerable to injury during gynecologic surgery, particularly when it is distorted by disease or anomalies. Some injuries are manifested early, but in other instances recognition of the damage may be delayed, especially if it is secondary to interference with the nervous or vascular supply to the ureterovesical area.

Intravenous pyelograms were obtained before and after surgery in 200 consecutive patients undergoing hysterectomy for benign uterine conditions, and in 151 patients both studies were normal. In 41 patients there were varying degrees of hydronephrosis, which reverted to normal after hysterectomy in 37. In nearly half of the cases pelvic tumors produced an extrinsic pressure defect on the dome of the distended urinary bladder, and in a large number this defect was still demonstrable postoperatively. Urinary calcification was present in 3 cases.

The postoperative pyelograms showed that the ureter was injured 5 times, an incidence of 2.5 per cent. In all o these cases there was unilateral hydroureter and/or hydronephrosis of varying degree, with few or no clinical findings pointing to this complication. The obstruction was temporary and subsided spontaneously

in 2 cases; in a third it was minimal, persistent, and asymptomatic. In 1 patient the obstruction was relieved by surgical freeing of the ureter. One patient had a double right collecting system and postoperatively hydronephrosis of the upper right renal complex only was demonstrated, while the lower pelvis and ureter were normal. The reason for the temporary nature of these obstructions is difficult to assess accurately, but the authors conjecture that it is due to dissolution of absorbable catgut, release of tension in nearby structures, or spontaneous recovery from a crushing injury.

In view of the tendency toward spontaneous improvement of ureteral injuries incident to hysterectomy, a policy of close observation may be adopted when such an injury occurs. If, however, obstruction shows no amelioration or there are other urinary tract complications, operative treatment is indicated. The most alarming feature of this type of ureteric injury is the innocuous symptomatology; in the 5 cases in the series reported here it is doubtful whether the injuries would have been discovered if pyelography had not been employed.

Sixteen roentgenograms; 2 tables.

IRVING J. WEIGENSBERG, M.D.
University of Pennsylvania

Pulmonary Embolization Following Urethrography with an Oily Medium. Aaron Hardy Ulm and Ely C. Wagshul. New England J. Med. **263:** 137–139, July 21, 1960. (New York University College of Medicine, New York, N. Y.)

The authors report 2 cases in which pulmonary embolization occurred after inadvertent injection of Lipiodol into the venous circulation during urethrography. In both patients acute pneumonitis ensued. Serial roentgenograms of the chest were obtained to determine the time required for ultimate clearing of the lung fields. This amounted to about a month in one case and less than two weeks in the other.

The course of the pulmonary complication and the roentgenographic findings are not necessarily parallel. The persistence of roentgen changes long after subsidence of pulmonary symptoms suggests that a large part of the initial radiographic change in the lung may be attributed to the radiopacity of the provoking material. The use of Lipiodol for urethrography is condemned.

Four roentgenograms.

THEODORE E. KEATS, M.D.
University of Missouri

Pyelorenal Uptake in the Normal and Pyelonephritic Kidney. Charles H. Nicolai. J. Urol. **84:** 14–16, July 1960. (607 N. Grand Blvd., St. Louis 6, Mo.)

The pyelorenal fluid exchange properties in the normal and pyelonephritic kidney were studied by comparing the uptake of radioactive iodine in the form of sodium iodide-131 from the obstructed renal pelvis, in the kidneys of 8 normal rabbits, and in 8 with pyelonephritis (laboratory-produced).

The test isotope of known quantity and quality was introduced into the renal pelvis without increasing the intrarenal pressure, and the radioactivity of the peripheral blood was measured at one-hour intervals, with a well-type scintillation counter. The results showed a significant decrease in pyelorenal backflow in the diseased kidney. This points to a decreased circulation, which appears to be lymphatic. Work is now under way to determine what lymph channels are obstructed because of pyelonephritic changes.

Four figures.

CORRINE FARRELL, M.D.
University of Pennsylvania

Backflow Patterns in Experimental Chronic Hydronephrosis. Marvin Kazmin, Lester Persky, and John P. Storaasli. J. Urol. **84:** 10–13, July 1960. (Western Reserve University School of Medicine, Cleveland 6, Ohio)

The authors designed a group of experiments to determine whether or not backflow occurs in the chronic phase of hydronephrosis, to attempt to quantitate it relative to earlier studies (see, for example, J. Urol. **75:** 190, 1956. Abst. in Radiology **67:** 922, 1956), and, if possible, to determine the route of backflow as shown by radioautographs.

Three groups of dogs were studied after ligation of the left ureter, with periods of obstruction persisting for forty-eight hours, seventy-two hours, and seven days. The animal was operated upon again at the end of the ligation period and, after aspiration of the contents of the renal pelvis, isotonic saline, containing 250 microcuries of radioactive iodinated albumin, was instilled, restoring the original volume and intrapelvic pressure. Samples of the peripheral blood were drawn from the jugular vein at five-minute intervals for one hour, and the radioactivity measured with a scintillation counter. In selected animals radioautographs were obtained.

Analysis of the results revealed that reflux of pelvic contents occurred consistently in each group, paralleling in amount that determined in studies made with acute preparations. Radioautographs suggested a pyelotubular route of backflow.

One radioautograph; 3 graphs; 3 tables.

WALLACE T. MILLER, M.D.
University of Pennsylvania

MISCELLANEOUS

The Cause and Treatment of Edema of the Arm Following Radical Mastectomy. Magnus I. Smedal and James A. Evans. Surg., Gynec. & Obst. **111:** 29–40, July 1960. (Lahey Clinic, Boston 15, Mass.)

A swollen arm was found in 57 per cent of all patients seen at the Lahey Clinic who had undergone radical mastectomies in 1958. While either surgical or radiation destruction of lymphatics has been suggested as a primary cause, the authors find no good evidence to support such contention. Their clinical observations lead them to conclude that the main causative factor of arm edema following radical mastectomy is thrombophlebitis with concomitant inflammatory obstruction of the vascular sheath lymphatics.

Of the 27 patients referred to the Lahey Clinic in 1958 for radiotherapy, 85 per cent had postoperative clinical evidence of phlebitis and swelling of the arm; 45 per cent of this group had swelling of the arm before radiotherapy was started.

Signs of phlebitis noted included: (1) soreness in the distribution of the brachial vein within a few days after operation, (2) tenderness elicited along the axillary and brachial veins, (3) swelling of the upper arm, (4) cyanosis of the arm, sometimes paleness, (5) development of visible collateral veins, (6) visible distention of subcutaneous lymphatics, (7) pain on stretching the involved vein, by extending the elbow (similar to Homans' sign), and (8) pulmonary embolism (2 cases).

In 1957 and 1958 venography was performed on 27 patients with swollen arms. Positive evidence of phlebitis was demonstrated in 25. Five abnormalities in the venogram were considered typical of thrombophlebitis: (1) obstruction, (2) a filling defect in the lumen of a vein, (3) filling of collateral veins, (4) retrograde filling of veins, and (5) slow emptying.

The importance of recognizing postoperative thrombophlebitis of the arm lies in the possibility of prophylaxis and treatment by anticoagulants and clot solvents that are now available.

Eighteen roentgenograms; 2 photographs.

DAVID E. KUHL, M.D.
University of Pennsylvania

RADIOTHERAPY

The Advantages of Employing Mixed High Energy X-Ray and Electron Beams in Radiation Therapy. Noel H. Gale and G. S. Innes. Brit. J. Radiol. **33:** 261–264, April 1960. (The University, Manchester, England)

From experimental depth-dose measurements with a 15-million-volt electron accelerator, the authors suggest that advantages can be derived from the use of a combination of high-energy x-rays and electrons in patient therapy. The electron beam is most useful for the treatment of lesions beginning near the surface and extending to a depth not greater than 4 cm., beyond which rapid attenuation of the beam occurs. The 15-million-volt x-rays yield a maximal energy distribution from 1.5 to 5.7 cm. below the skin. A mixture of the beam enlarges the isodose area in the superficial regions, while sparing the deeper structures from the high radiation levels of a pure x-ray beam.

Aside from mixed beams produced by superimposing x-ray and electron beams through the same skin portal, there is the possibility of using x-ray and electron fields which overlap only in part, producing isodose distributions of T, L, or H shape. The two types of beam can further be employed for adjacent fields, as in the treatment of breast carcinoma and the internal mammary glands.

In practice, mixed beam therapy may be accomplished in one of two ways. In the first, pure x-ray and electron beams would be used, the patient being given successive amounts of the two radiations in the correct proportions to secure the desired isodose distribution. In the second method, a mixed beam would be produced and the patient treated directly with it.

The second method poses some difficulties, namely, the difference in the dosage rates of electrons and x-rays and the necessity of flattening both beams simultaneously. It would seem possible, however, to produce a mixed x-ray and electron beam which has a flat isodose curve, and with the correct percentages of x-rays and electrons, by using a shaped x-ray target with a hole drilled through it, across which hole is placed a scattering foil. Such a target has been made, and measurement of the beam distribution with and without the axial hole indicates that the mixed beam so produced is composed of approximately 40 per cent of electrons and 60 per cent of x-rays.

Eight figures.

EVERETT H. SCHULTZ, JR., M.D.
University of Florida, Gainesville, Fla.

A Comparison of Theoretical and Experimental Spectral Distributions of Scattered X-Rays. D. V. Cormack. J. Canad. A. Radiologists **11:** 40–43, June 1960. (Saskatoon Cancer Clinic, Saskatoon, Sask., Canada)

A substantial portion of the absorbed dose from an x-ray beam is due to scattered radiation. An expression of the quality or "effective wave length" of the radiation at any point in the depth therefore requires knowledge of the spectrum of both the primary and scattered rays. Recent calculations of Bruce (Bruce and Johns: Brit. J. Radiol. Suppl. 9, 1960) make it possible to calculate the scattered spectrum for any of a wide range of depths, areas, and focal-skin distances, once the spectrum of the incident primary radiation is known. The author checked these theoretical calculations against actual laboratory measurements under a number of conditions and found the two in satisfactory agreement. It thus appears that Bruce's data may be used with confidence in calculating integrated scattered spectra from known primary spectra.

Five graphs.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

RADIOISOTOPES

Measurement of Myocardial Blood Flow. Radioisotope Techniques Used in Patients with Normal and Arteriosclerotic Hearts After Infarction. Philip C. Johnson and Gunnar Sevelius. J. A. M. A. **173:** 1231–1233, July 16, 1960. (P. C. J., Methodist Hospital, Texas Medical Center, Houston, Texas)

With a scintillation detector placed on the chest wall the first passage of a radioactive bolus through the right and left sides of the heart and through the myocardial circulation can be monitored and, on the basis of the time activity curve obtained, the myocardial blood flow and cardiac output can be determined. The authors used this technic to test the effect of a long-acting and a short-acting nitrate compound (pentaerythritol tetranitrate, PETN, and nitroglycerin, respectively) on myocardial circulation and cardiac output in patients with and without arteriosclerotic heart disease.

Three groups of patients were used in the study. Groups I and II were controls and consisted of 8 middle-aged women and 11 middle-aged men, of average height and weight, hospitalized for diseases not related to the cardiovascular system and with no evidence of cardiovascular disease. Ten patients with diagnoses of previous myocardial infarction comprised Group III. About 30 per cent of these had angina on exertion at the time of the study. No patients in cardiac failure were included. Radioiodinated human serum albumin was used as the tracer substance to determine cardiac output; for all other curves radioactive iodopyracet (Diodrast) was employed as the tracer.

Myocardial blood flow and cardiac output were determined in each patient before and after the sublingual

administration of 0.6 mg. of nitroglycerin and similarly after an oral dose of 20 mg. of PETN. It was found that myocardial blood flow is significantly (50 per cent) decreased in patients with coronary artery disease who receive no therapy. A significant correlation exists between the responses, in terms of increased myocardial blood flow, to sublingual nitroglycerin and to oral administration of PETN in individual patients. Ten minutes after the administration of 0.6 mg. of nitroglycerin, there is an increase in myocardial blood flow, without change in cardiac output, in patients with arteriosclerotic heart disease. PETN produces a prolonged increase in myocardial blood flow beginning within one hour after infiestion and lasting up to five hours, without producing changes in cardiac output, in patients with arteriosclerotic heart disease with previous infarction.

In all groups of patients, normal and arteriosclerotic, a significant correlation ($r = 0.68$) was found between the increase in coronary blood flow produced by nitroglycerin and that produced with PETN. It might be possible to anticipate, from the short-acting clinical response to nitroglycerin, the clinical usefulness of PETN in any individual patient.

Intracardiac Injection of Radioactive Krypton. Clinical Applications of New Methods for Characterization of Circulatory Shunts. Robert T. L. Long, Eugene Braunwald, and Andrew G. Morrow. Circulation **21:** 1126–1133, June 1960. (National Heart Institute, Bethesda, Md.)

During the course of clinical studies in which the radioactive gas krypton (Kr^{85}) was inhaled (Am. J. Med. **26:** 508, 1959. Abst. in Radiology **75:** 150, 1960), it was found that the isotope is slightly soluble in normal saline. Following the injection of krypton in solution into the right side of the heart, approximately 95 per cent is cleared during one passage through the pulmonary circulation. Arterial blood activity is low when the Kr^{85} is injected in the absence of, or distal to, the origin of a right-to-left shunt. When injected proximal to the origin of such a shunt, however, a fraction of the Kr^{85} bypasses the pulmonary capillary bed and appears in arterial blood.

The authors report their experiences with intracardiac injection of Kr^{85} in 48 patients. In all the presence or absence of a shunt was verified by the findings at operation or autopsy or other diagnostic procedures, including selective angiography, the results of nitrous oxide or Kr^{85} inhalation tests, and dye-dilution curves.

Thirty to 50 μc Kr^{85} were injected into the right heart, and arterial blood was sampled during the next fifteen seconds. In 19 patients without right-to-left shunts, the activity per milliliter of arterial blood was always less than 9.0×10^{-6} and averaged $2.5 \pm 2.6 \times 10^{-6}$ of the total radioactivity injected. In 9 patients with right-to-left shunts, the radioactivity per milliliter of arterial blood always exceeded 8.2×10^{-6} and averaged $30.1 \pm 12.2 \times 10^{-6}$ of the total activity injected.

Following injection into the left heart, proximal to the origin of a left-to-right shunt, in 22 patients, the Kr^{85} appeared in the expired gas in an average of 4.0 $\pm$ 1.6 seconds. However, after injection distal to the origin of a left-to-right shunt in 18 patients, the appearance of Kr^{85} in the expired gas was delayed to a mean of 15.0 $\pm$ 5.0 seconds.

The authors consider the test sufficiently sensitive to detect and localize even small cardiac shunts.

Six cases illustrating the applications of the method are reported.

Five figures. ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Studies with Chlorothiazide Tagged with Radioactive Carbon (C^{14}) in Human Beings. Herbert R. Brettell, Jerry K. Aikawa, and Gerald S. Gordon. Arch. Int. Med. **106:** 57–63, July 1960. (J. K. A., University of Colorado Medical Center, 4200 East Ninth Ave., Denver 20, Colo.)

Chlorothiazide (Diuril), a nonmercurial diuretic agent, has been shown clinically to be effective in the treatment of hypertension and various disease states associated with retention of water and electrolytes. The authors attempted to delineate its behavior, by labeling it with C^{14}, in 10 normal adults, in 10 patients with congestive heart failure, in 6 with hepatic disease, and in 4 with renal disease. The substance was given orally or intravenously and serial blood and urine specimens were analyzed for radioactivity.

In normal adults the radioactivity was recovered completely in the urine within twenty-four hours after an intravenous injection of tagged chlorothiazide; in the same time interval 33 to 58 per cent of an orally administered dose was excreted in the urine. Patients with cardiac, renal, and hepatic diseases showed a lower cumulative excretion of radioactivity. The oral dose of 500 to 1,000 mg. in normal persons usually produced a urine flow of at least 200 ml. an hour, suggesting that the amount was sufficient to produce diuresis in the absence of diseases affecting the heart, kidneys, or liver.

The results obtained in the patients with heart failure suggested a rough correlation between the clinical severity of the disease and the degree of impairment in the urinary excretion of chlorothiazide.

The renal excretion of radioactivity was extremely low in patients with renal glomerular disease. It would seem that neither chlorothiazide nor any other diuretic agent would be effective unless a certain minimal amount of functional renal tissue remains.

Of the four groups studied, the patients with liver disease showed the poorest diuretic response to chlorothiazide and the lowest serum concentration of the drug, possibly because of poor gastrointestinal absorption when the drug was given orally.

The study suggests that the renal excretion of radioactivity given orally or intravenously as C^{14}-chlorothiazide is in inverse ratio to the severity of diseases affecting the heart, kidneys, or liver, but that the factors responsible for this uniformly poor response may vary with different pathologic conditions. It remains to be determined whether the parenteral administration of chlorothiazide to patients with severe hepatic and cardiac disease will induce diuresis when large oral doses fail to do so.

Four figures; 1 table.

Radioactive Iron Techniques in Clinical Practice. Walter Lentino, Carl Collica, and Sidney Rubenfeld. J. A. M. A. **173:** 481–487, June 4, 1960. (Bellevue Hospital, New York, N. Y.)

The rate at which intravenously injected iron disappears from the blood depends partly on the rate at which iron is being used for the production of fresh erythrocytes in the bone marrow. The injection of radioactive iron (Fe^{59}) has proved to be a convenient

means of measuring the rate of disappearance of iron from the plasma and its uptake by the erythrocytes.

The authors describe the radioiron technic employed in the Radioisotope Department of Bellevue Hospital, New York, and indicate its usefulness in clinical practice. After intravenous injection of about 4 μc of radioactive iron citrate, whole blood samples are taken at five-, fifteen-, thirty-, sixty-, ninety-, and one-hundred-and-twenty-minute and eight-day intervals. By directly counting 4-c.c. aliquots, the plasma clearance one-half time and the eight-day red blood cell uptake are obtained. The normal plasma clearance one-half time is sixty-five to one hundred and ten minutes; the eight-day red blood cell uptake is 95 to 100 per cent.

The justification for interpreting radioactive iron-tracer tests as indexes of erythropoiesis are reviewed and objections to the test are challenged. The results have been shown to be useful in the diagnosis of aplastic anemia, iron deficiency anemia, leukemia, and polycythemia. Since continuing losses of blood and variations in the iron stores of the body affect the results, intelligent interpretation is required.

Four figures; 2 tables.

The Life Cycle of the Erythrocytes of Irradiated Animals Studied by Means of Fe^{59}. B. Bellion and L. Resegotti. Minerva nucleare **3:** 241–244, July-August 1959. English translation in Panminerva med. **2:** 342-344, July-August 1960. (Istituto di clinica medica dell'Università, Turin, Italy)

In a study of the relative biological efficiency (RBE) of radiations of the same type, but with different energy, an assessment of the alteration of erythropoiesis was made by studying the incorporation of radioactive iron into the circulating erythrocytes before and after irradiation. The investigation was carried out on 12 adult rabbits weighing 2,400 to 3,500 grams. Three animals were exposed to a single dose of 200 r of whole-body x-irradiation by means of a conventional 200-kv apparatus twenty-four hours before the administration of the radioactive iron. Two other groups, of 3 animals each, received an equal dose of 200 r of whole-body x-irradiation by means of a 31-Mev betatron twenty-four hours before and seventy-two hours after the administration of the tracer, respectively. One animal (No. 10) was intravenously injected with 15 ml. of plasma exposed *in vitro* to 2,000 r of 200-kv x-rays twenty-four hours before the administration of the radioactive iron. Two animals were kept as controls. They were injected with Fe^{59} but were not exposed to irradiation. Particular care was taken in determining the mean doses of 31 Mev and 200 kv x-rays.

The rate of disappearance of the Fe^{59} atoms from the plasma was decreased in the irradiated animals: to a greater extent in those exposed to 200 kv than in those irradiated with the betatron. The lowest rate was found in Animal No. 10 but, because this experiment was carried out on only 1 animal, the result is of limited value. Only in the animals exposed to low-energy x-rays was the incorporation of the tracer into the erythrocytes markedly decreased twenty-four hours after the injection of the isotope. The decrease was less evident at forty-eight and seventy-two hours.

The findings suggest a lower biological efficiency for the betatron x-rays than for the 200-kv x-rays. Where the animals were exposed to betatron irradiation seventy-two hours after administration of the tracer dose, the irradiation affected not only erythropoiesis but also the circulating erythrocytes. The latter effect could be due to changes in the capillary vessels as a result of the irradiation.

An experiment in which irradiated plasma was intravenously injected in 1 rabbit suggested that the indirect effect of irradiation plays a great role in the inhibition of erythropoiesis.

The Use of Cr^{51} Labelled Red Blood Cells in the Study of Splenomegaly and the Seats of Haemocatheresis. A. Fieschi, L. Pannacciulli, and A. Tizianello. Minerva nucleare **3:** 85, April 1959. English translation in Panminerva med. **2:** 334–341, July-August 1960. (Istituto patologia speciale medica, Genoa, Italy)

The recent use of tracer technics has made it possible to investigate the conditions under which the spleen is enlarged and the role of that organ in the destruction of the red cells. These investigations are easily carried out by a single basic method, namely, injection of Cr^{51}-labeled erythrocytes. Dilution curves of the tracer may be evaluated at different times, demonstrating the possible presence of red cell fractions with different life cycles; the volume of the spleen may be determined, as well as the degree of hemolysis and the role of the spleen in the destruction of the red cells.

In normal subjects the maximum distribution of the tracer is attained two to three minutes after injection. In 16 patients with splenomegaly the authors found a mixing time ranging from ten to thirty minutes, with a mean value of seventeen minutes. The erythrocyte mass value was greater than might be supposed, possibly because of the enlargement of the spleen, which also induces a proportional increase in its vascular bed. In splenomegaly, a significant fraction of erythrocytes is removed from circulation.

The role of the spleen in the destruction of red blood cells can be studied with Cr^{51}-labeled erythrocytes, by following the distribution of the radioactivity of the red cells with directional counters. When the red cells are destroyed, the radioactivity passes into the organs. While this method does not permit a quantitative measurement of radioactivity, owing to the technical defects of surface counting, it is suitable for comparative measurements in various organs and for serial determinations in the same organ. The highest uptake values are reached on the day corresponding to the half-life of the Cr^{51}-labeled erythrocytes. At that time the ratio between the maximum uptake in the spleen and liver can be assessed. In splenomegalic patients the spleen/liver ratio is high in the first few days, a fact which must be borne in mind when assessing the spleen/liver ratio on the half-life day.

In normal subjects the rate of destruction of red blood cells is such that the inflow of radioactivity in the spleen is balanced by the outflow and, after a slight increase, the radioactivity curves of both spleen and liver are flat: the spleen/liver ratio is about 1.

In the majority of patients with increased hemolysis, the radioactivity is mostly taken up in the spleen. The spleen/liver ratio is usually greater than 2 and is sometimes as large as 8 or 9. (It must be borne in mind that surface counting does not provide information on the total radioactivity of the two organs.) In some cases of acquired hemolytic anemia, the liver uptake increases with the spleen uptake and it is conceivable that in these patients the liver plays an important part in blood destruction. This method for tracing the site of

red cell destruction permits recognition of the cases of acquired hemolytic anemia with high spleen uptake and spleen/liver ratio. In these cases splenectomy can be performed with some hope of success, but it should not be undertaken when the liver uptake is high.

In 7 cases in which splenectomy was done, the best results were achieved when the spleen uptake and the spleen/liver ratio were high. In 1 case treatment with prednisone hardly affected the degree of hemolysis, while splenectomy induced a normalization which was maintained at the time of this report, one year later.

The spleen uptake can be used as a check of the erythrocyte life span. If a rapid disappearance of radioactivity from circulation is not accompanied by a proportional increase of activity in the spleen, hemorrhage must be suspected. When a loss of labeled red cells from circulation is due to intravascular hemolysis, the situation has great clinical significance.

A thorough study of the site of blood destruction following splenectomy has not yet been made, but the authors report that in a patient who was splenectomized eleven years ago radioactivity studies suggest that the liver has taken over the role of the spleen in blood destruction.

In patients with splenomegaly, an increased erythrocyte mass can be directly determined. The tracer method can be used, moreover, when a mass of unknown nature is found in the left hypochondrium; the finding of an increased erythrocyte volume would suggest that the mass is splenic. The routine use of this technic will provide useful information on many important points of hematologic and splenic pathology.

Five figures; 3 tables.

Excretion of Radioiodine in Human Milk. John C. Weaver, Michael L. Kamm, and R. Lowry Dobson. J. A. M. A. **173:** 872–875, June 25, 1960. (2640 Telegraph Ave., Berkeley, Calif.)

The possibility that I^{131} administered to a lactating woman might reach the nursling in harmful amounts was studied in 6 euthyroid nursing mothers, most of whom were already in the process of weaning their babies. Radioactive iodine was given by mouth in doses of 10 μc to 5 mothers and of 30 μc to 1 just after the final breast feeding. Within forty-eight hours after administration, 1.4, 3.9, 0.14, 0.03, 6.2, and 26.8 per cent of the amounts given, respectively, appeared in the milk which was stripped manually from the breasts. Most of the I^{131} was secreted during the first twenty-four hours. The percentage of administered dose excreted in the milk is roughly in proportion to the quantity of milk produced. The greatest hazard to the nursing infant will thus occur when the mother produces large quantities of milk and makes little or no use of supplement.

Before administration of radioactive iodine to women of child-bearing age, they should routinely be questioned about lactation. Nursing should be interrupted for at least twelve and preferably for twenty-four hours or, in the case of a large diagnostic or therapeutic dose, until measurements indicate that the I^{131} content of the milk is no longer significant.

Two figures; 3 tables.

The Design of Caesium Sources for Teletherapy. W. S. Eastwood. Brit. J. Radiol. **33:** 243–245, April 1960. (Atomic Energy Research Establishment, Harwell, Berkshire, England)

This article is in the nature of an historical account of the development of cesium sources for teletherapy under the direction of the Atomic Energy Authority of Great Britain, beginning in 1952. Cesium metal was held to be too reactive for the purpose and cesium chloride and sulfate were therefore considered. The chloride has a slightly greater activity per unit volume but was thought more likely to yield corrosive products if decomposed by its own radiation. The sulfate was therefore employed.

The specific activity of fission-product cesium is low in comparison with Co^{60}; a volume of 20 to 30 c.c. is required to give a clinically useful dose rate at a suitable source-skin distance. An active source diameter of 2.7 cm. was chosen, small enough to maintain a reasonable limit on penumbra but wide enough that length and self-absorption of the source would not be excessive.

Sources were produced by melting and pouring rather than by compressing tablets from the salt. After several trials, monel capsules were found more satisfactory than platinum as a container, due to the lower absorption of gamma radiation by monel.

Two illustrations.

EVERETT H. SCHULTZ, JR., M.D.
University of Florida, Gainesville, Fla.

Physical Aspects of the Use of Caesium Fission Products in Teletherapy. B. M. Wheatley. Brit. J. Radiol. **33:** 246–250, April 1960. (Royal Cancer Hospital, London, S. W. 3, England)

When radioactive cesium is chemically separated from the fission products of uranium, it is found to consist of β-active Cs^{135} and stable Cs^{133}, in addition to γ-active Cs^{137}. Some γ-emitting Cs^{134} is also present as a result of transformation of Cs^{133} by neutron capture in the reactor. Since the half-life of Cs^{134} is short (2.3 years), it contributes to the dose-rate from the mixed source only in the first few years. Therefore, output checks on cesium units should be made frequently during the early years of operation.

Because of self-absorption and absorption in the monel capsule, the practical output of cesium γ-rays from a 1,000 curie source is similar to the theoretical output from a point source of approximately 680 curies. In addition to the 660 kev γ-rays, there are contributions arising from scattering within the source and from bremsstrahlung, having a peak energy near 300 kev.

Transmission of γ-radiation through the shielding of the treatment head is greater than would be expected from calculations based on the mass absorption coefficients for narrow beams, because of diffuse scattering in the entire shielding area. Equations for percentage transmission under these conditions, and for dose-rate at the surface of the shield, are given.

Protective walls for the cesium beam are designed in accordance with standards such as are presented in N.B.S. *Handbook* 54.

Six figures; 1 table.

EVERETT H. SCHULTZ, JR., M.D.
University of Florida, Gainesville, Fla.

A Caesium 137 Beam Therapy Unit. I. Physical Aspects. B. M. Wheatley, J. C. Jones, and T. C. Sinclair. **II. Clinical Impressions.** E. D. Jones. Brit. J. Radiol. **33:** 251–260, April 1960. (J. C. J., Royal Cancer Hospital, London, S. W. 3, England)

A cesium-137 source for teletherapy was installed at the Downs Branch of the Royal Marsden Hospital (London) in 1956. A source holder and switching

mechanism, similar in principle to those used for cobalt sources, were designed for the cesium source. The concrete wall of the treatment room which receives the primary beam was made 24 inches thick and faced with brick. The entire room was ventilated through a filter system which was tested at intervals for possible leakage from the radioactive source. During a year of operation, 0.1 microcurie of Cs^{137} was extracted by the filter.

From the 1,500-curie source, an output of 23.9 r/minute in air at 40 cm. was obtained. The half-value layer was measured at 11 mm. of copper, or 5.5 mm. of lead. Measurements in phantoms indicated that bone absorption of the gamma-radiation of Cs^{137} was approximately one-third that of orthovoltage x-radiation. The depth of maximum dose in tissue was only 1 mm., as compared with 6 mm. for cobalt teletherapy.

A source-skin distance of 40 cm. was necessary to maintain an adequate dose-rate and to limit penumbra, although at this short distance it was sometimes difficult to position the unit relative to the patient.

In clinical practice, early skin reactions were significantly less with Cs^{137} therapy than with orthovoltage x-rays. An impression was gained that later reactions with cesium were also less marked. The constitutional reactions of patients treated with the cesium unit seemed less than with conventional therapy, compatible with the fact that the integral dose is lower than that received by an equivalent treatment with orthovoltage x-rays.

While the cesium unit does not compete with supervoltage machines for the treatment of deep-seated lesions, it does give some advantages over conventional therapy, especially for treating comparatively superficial lesions lying deep to bone.

Eleven illustrations, including 1 roentgenogram; 5 tables. EVERETT H. SCHULTZ, JR., M.D.
University of Florida, Gainesville, Fla.

Estradiol Reduces Incorporation of Radioactive Sulfate into Cartilage and Aortas of Rats. Robert E. Priest, R. Marlene Koplitz, and Earl P. Benditt. J. Exper. Med. **112**: 225–236, July 1, 1960. (University of Washington Medical School, Seattle, Wash.)

An attempt was made to determine whether one gonadal steroid, estradiol, influences the metabolism of connective tissue. The incorporation of sulfate labeled with S^{35} into the hyaline costal cartilage and aorta of male rats, both *in vivo* and *in vitro*, was used as a specific measure of metabolic activity of sulfated mucopolysaccharides.

Young adult male rats were divided into two groups of 6 on the basis of weight. Those in one group were given daily injections of 0.33 mg. of estradiol benzoate in sesame oil; the other 6 received an equal volume of sesame oil. After three weeks 100 μc of S^{35} as sulfate was injected intraperitoneally into each rat. Twenty-four hours later the animals were sacrificed; the tissues were removed and weighed and assayed for radioactivity. Incorporation into costal cartilage of animals treated with estradiol averaged 34 per cent of the amount found in animals not so treated. This difference is highly significant ($p < 0.001$) despite the wide dispersion of observations in the control group. The difference between incorporation into aortas of treated and untreated animals is not impresssive and could easily be due to chance.

An *in vitro* technic for observing incorporation of sulfate into surviving tissues was devised. Again adult male animals were treated with estradiol benzoate for three weeks. The tissues were then removed, incubated for four hours in a medium containing labeled sulfate, assayed for radioactivity, and compared with tissues from animals not treated with estradiol. The incorporation into costal cartilage of the treated groups was approximately half that of the control group.

In order to approximate the time necessary for the effect of estradiol to become apparent, male animals were injected daily for varying periods of time and their tissues, after four-hour incubation, were compared with those of untreated animals. No diminution in incorporation of sulfate into cartilage was demonstrable at the end of the first day, but was apparent by three days. Incorporation into aorta as well as cartilage seemed to be reduced after two and three weeks of treatment. The delay of more than a day in the case of cartilage and more than three days in the case of the aorta before the influence of estradiol became demonstrable by the technics employed suggested that the effect might be mediated through another hormone, or through some other secondary effect. Experiments were therefore undertaken to investigate some of the possibilities. It was found that the effect is not mediated through suppression of testosterone secretion and that the hypophysis is not necessary for the effect to be demonstrated.

Inhibition of experimentally produced coronary lesions has been shown in chickens and rats given estrogen. With the demonstration that estradiol influences the metabolism of arterial sulfate and probably of sulfated mucopolysaccharides, which are prominent components of the atherosclerotic lesion, the possibility that estrogenic hormones influence the development of the atherosclerotic lesions through changes in the metabolism of the arterial wall itself should not be ignored.

Four figures; 4 tables.

The Transfer of Strontium-90 from Mother to Fetus in Mice. Bo Holmberg, Arne Nelson, and Elsie Wallgren. Radiation Res. **12**: 167–172, February 1960. (Research Institute of National Defence, Sundbyberg, Sweden)

The transfer of Sr^{90} from mother to fetus in mice was studied after intraperitoneal injection of the isotope. The investigation included the time course of uptake at the end of gestation, the uptake at different stages of gestation, and the fetal uptake after mating at different intervals after the injection. The authors found that the ability of the fetus to take up strontium-90 appeared after the fourteenth day of gestation. Studies on the nineteenth day indicated an uptake continuing more than four hours after injection of the mother. In one experiment it was demonstrated that Sr^{90} injected in the mother was available to the fetus in undiminished quantity for at least four weeks.

Four figures; 3 tables. AUTHORS' SUMMARY

RADIATION EFFECTS

Factors Influencing Maximum Permissible Doses of Radiations. Gordon Richards Memorial Lecture, 1960. Robert S. Stone. J. Canad. A. Radiologisst **11:** 26–34, June 1960. (University of California School of Medicine, San Francisco, Calif.)

The author introduces this discussion of factors influencing maximum permissible doses of radiations by declaring his intention of interpreting the subject broadly and including some recent interpretations, explanations, and changes made in 1959 by the International Commission on Radiological Protection, of which he is a member. He is led to the following conclusions:

"The problem of establishing the doses to which various groups of the population can be exposed without injury to themselves or deterioration of future generations has become more difficult rather than more simple as more information has become available.

"Until it can be proved that there is a threshold for somatic effects, we cannot set maximum permissible doses that are absolutely safe.

"The theory of total additivity of all exposures to ionizing radiation so far as genetic effects are concerned is no longer entirely tenable for man, but until more is known all gonadal exposures must be kept to a minimum.

"The sensitivity of the embryo and foetus with regard to production of malformations and early childhood malignancies make women in the reproductive age a special hazard problem as occupational workers.

"A balance sheet of the good to be accomplished against the risks to be run shows heavy weighting in favor of the good in the instance of survey photoroentgenograms of the chest.

"The total medical radiation hazard has been overestimated, but because there are hazards, it is incumbent on radiologists to take all known precautions to keep the exposure of the gonads to the lowest possible level consistent with the medical needs of the patient."

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Acute Leukemia After Radioactive Iodine (I^{131}) Therapy for Hyperthyroidism. Thomas W. Burns, Raymond Vickers, and John F. Lowney. Arch. Int. Med. **106:** 97–100, July 1960. (University of Missouri School of Medicine, Columbia, Mo.)

The possibility that radioactive iodine may be carcinogenic in tissue other than thyroid is raised by reports of acute leukemia following use of the isotope for hyperthyroidism (see, for example, Pochin *et al.* Brit. J. Radiol. **29:** 31, 1956. Abst. in Radiology **67:** 792, 1956). Clinical and hematological data for 2 additional patients are presented in this paper, bringing to 10 the number of cases believed to have been reported. The time lapse from the date of radioactive iodine administration and the data of diagnosis of acute monocytic leukemia was seven years in the authors' Case I and six months in Case II. These time periods fall well outside the range of eighteen and twenty-four months previously noted. The first patient appeared retrospectively, however, to have been in a preleukemic phase for at least twenty months before the diagnosis of acute leukemia was made.

While no one would suggest that a causal relationship between acute leukemia and radioactive iodine has been established, it would seem that there is enough evidence available to make the possibility of such an association a matter of concern. The reassurances that have led to wide and liberal use of radioactive iodine therapy in hyperthyroidism need critical re-examination.

Three tables.

Studies on Radiation-Induced Mammary Gland Neoplasia in the Rat. III. Relation of the Neoplastic Response to Dose of Total-Body Radiation. V. P. Bond, E. P. Cronkite, S. W. Lippincott, and Claire J. Shellabarger. Radiation Res. **12:** 276–285, March 1960. (Brookhaven National Laboratory, Upton, N. Y.)

In previous studies from the Brookhaven Laboratory (Radiation Res. **12:** 81 and 94, 1960. Abst. in Radiology **76:** 701, 1961) it was reported that total-body x-or γ-irradiation of female Sprague-Dawley rats resulted in a high percentage of mammary gland neoplasia, and there was some indication that the response might be dose-dependent. The present experiments were designed to investigate the relationship between the neoplastic response of the breast and the dose of radiation over an extended dose range.

The dose dependency of the breast neoplasia response was studied in female Sprague-Dawley rats exposed to graded doses of acute total-body x-irradiation at forty days of age. The incidence of neoplasia scored at ten and a half to eleven months was linear on dose between 25 r (the lowest dose employed) and 400 r. The extrapolated curve passed through zero incidence at zero dose. Above 400 r, the incidence either remained constant or decreased.

Multiple neoplasms in single animals were observed, and histologically the neoplasms were adenocarcinomas, adenofibromas, fibroadenomas, and fibrosarcomas. The neoplasms depend on intact ovarian function for maximal incidence. The dose-effect results are discussed in terms of their adequacy for interpretation in terms of the mechanism of radiation-induced neoplasia.

It is emphasized that the data reported on the relation of dose and neoplasia of the rat breast cannot be extrapolated to other types of neoplasia or to other species. It is pointed out that linearity of response for a given tissue may be masked by dependence of the response on hormones or other factors in addition to irradiation.

Four figures; 2 tables.

Late Effects of X-Radiation. The Influence of Dose Fractionation on Life Span, Leukemia, and Nephrosclerosis Incidence in Mice. L. J. Cole, P. C. Nowell, and J. S. Arnold. Radiation Res. **12:** 173–185, February 1960. (L. J. C., U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

In an investigation of the long-term effects of irradiation in mice, a study was made (1) of the effect of x-ray dose fractionation on the incidence of nephrosclerosis; (2) of the incidence of leukemia at a high single radiation dose, without hematopoietic cell injection; and (3) of the effect of dose fractionation on leukemia incidence.

Female $(C57L \times A)F_1$ mice were divided into several groups which received the following treatment: *Group*

I, single exposure to 690 r of x-rays (LD 35); *Group II*, 690 r (single exposure) plus an injection of spleen cells from normal young (C57L X A)F_1 mice; *Group III*, exposure to 348 r plus a second 348-r dose eight weeks later; Group IV, four separate doses of 174 r given nineteen days apart; Group V, eight doses of 85 r given eight days apart; Group VI, nonirradiated controls. The mice were maintained for the duration of their natural life span and studied for late effects.

The highest incidence of leukemias was observed in Group V animals (39 per cent) as compared to 12.5 per cent incidence in Group I mice. The earliest occurrence of leukemias (at twelve months of age) was seen in the Group V mice.

The effect of radiation dose fractionation with respect to the incidence of nephrosclerosis is opposite to that on the occurrence of leukemia. Thus, the mice exposed to a single dose of 690 r (Group I) showed a high incidence of this late kidney lesion (53 per cent), whereas those in Group V showed a frequency of only 5 per cent, essentially identical with that of the nonirradiated mice. In general, dose fractionation decreased the occurrence of graying; Group V mice exhibited no graying.

The incidence of adenomatous hyperplastic gastrointestinal lesions was definitely reduced in mice receiving 85 r X 8 dose fractionation (Group V) as compared to the group receiving 690 r in a single exposure (Group I).

The nonirradiated mice had a mean life span of twenty-six and a half months and a maximum longevity of thirty-six months. All of the irradiated animals exhibited a shortened life span. The greatest decrement in life span was observed in the mice in Group V; the median life span in this group was only fifteen months as compared to a value of twenty-one months in the mice receiving the same total dose (690 r) in a single exposure.

The relevance of the above findings to the problem of radiation-induced aging is discussed.

Four figures; 4 tables.

Survival Time Following Massive Fractionated Irradiation. Howard L. Andrews. Radiation Res. **12:** 185–201, February 1960. (National Cancer Institute, Bethesda, Md.)

Mice, rats, hamsters, and guinea-pigs were subjected to supralethal doses of x-rays, delivered in two equal doses separated by a variable time interval. Survival time was studied as a function of interval between doses, for a constant total dose in each species. In general, fractionation reduced the effect of a given dose on survival time, although the pattern varies with the species. The reduced effectiveness is partly due to repair processes and partly due to irradiation wasted because it is absorbed by already doomed tissues.

Five figures. AUTHORS' SUMMARY

An Analysis of the $LD_{50/30}$ as Related to Radiation Intensity. L. C. Logie, M. D. Harris, R. E. Tatsch, and E. N. Van Hooser. Radiation Res. **12:** 349–356, April 1960. (School of Aviation Medicine, USAF, Randolph AFB, Texas)

Co^{60}-irradiation was administered to groups of rats in doses covering a 2000-fold span of dose rates. The LD 50/30 at five different intensities was determined, and an empirical equation relating LD 50/30 to intensity presented. Within the confines of two stated postulates, three equations were developed, relating repair to a time-intensity function. Each appears to predict about equally well within the narrow confines around an LD 50/30 dose.

The intensity of the administered irradiation and the biologic end point LD 50/30 in this study show a high degree of correlation. This offers a method for quantitative predictions of an effective dose based on intensity.

Two figures; 1 table.

Incidence of Mortality and Dose-Response Relationship Following Partial-Body X-Irradiation of the Rat. A. Dunjic, J. Maisin, P. Maldague, and H. Maisin. Radiation Res. **12:** 155–166, February 1960. (University of Louvain, Belgium)

The incidence of mortality and dose-response relationship for the early and late deaths following irradiation of the head, thorax, and abdomen of rats exposed to single doses of x-rays are given. The radiosensitivity of different biological systems involved after partial-body irradiation is compared. The implications of the mortality data following partial-body irradiation for the interpretation of the shortening of life span after whole-body irradiation are discussed.

Six figures; 2 tables. AUTHORS' SUMMARY

Radiation Injury: Adrenocortical and Gastric Responses in the Rat. D. G. Baker, C. G. Hunter, and E. Schönbaum. Radiation Res. **12:** 409–416, April 1960. (University of Toronto, Toronto, Ont., Canada)

Within approximately one hour after exposure of rats to 500 r, the earliest objective signs of the acute radiation syndrome are observed. When searching for methods to elucidate the role of the adrenal cortex in the syndrome, it did not appear possible to measure the corticosteroid output of the rat adrenal *in situ* without grave interference by anesthesia and trauma; the study of steroid formation by the isolated rat adrenal was chosen as the most suitable procedure. Some "nonspecific stress" responses, in particular those associated with the injury sustained by the gastrointestinal tract, were studied as well.

Both fasted and nonfasted male rats of the Wistar strain were subjected to either whole-body x-irradiation (500 and 700 r) or sham treatment. At various times, measured from the commencement of the irradiation procedure, animals were killed. From one hour to four days after exposure to the irradiation, no changes were demonstrated in comparative studies of steroid formation *in vitro* and of ascorbic acid concentration of adrenal tissue. In rats fasted overnight and sacrificed fifteen, thirty, or forty-five minutes after irradiation, some stimulation of the adrenal cortex was noted. This occurred whether the rats were irradiated or sham-treated. Irradiation increased the weight of the stomach contents of rats within forty-five minutes of exposure.

Three figures; 2 tables.

The Indirect Effect of Irradiation on Embryonic Development. I. Irradiation of the Mother While Shielding the Embryonic Site. Robert L. Brent and Mary M. McLaughlin. J. Dis. Child. **100:** 94–102, July 1960. (Jefferson Medical College, Philadelphia 7, Penna.)

An attempt was made to distinguish between the effects of indirect and direct irradiation on teratogene-

sis of the rat. The direct effects were obtained by total irradiation of the pregnant rat, and the indirect by irradiating the mother but not the uterus, on the ninth day of gestation. Malformations of the embryo were found when the mother was given total-body x-irradiation of 25 to 100 r, and 100 per cent mortality was obtained at dosages of 200 r and over.

Four groups of rats, pregnant for nine days, were tested: the control group and three experimental groups receiving progressively increasing dosages of radiation. Protection of the embryo in the group which received 400 r total-body irradiation was obtained by placing a lead shield over the uterus after operative exposure. In the other two groups irradiation was limited to the upper half of the body because of the inability to shield the uterus adequately when the higher dosages (1,000 and 1,400 r) were given. The same operation for exposure of the pregnant uterus was performed in all groups.

Although fetal mortality, maternal weight gain and mortality, and fetal growth varied according to the amount of radiation delivered to the mother, no congenital malformations were produced in any of the experimental groups.

The conclusions are that direct irradiation of the embryonic site, not the indirect effect of irradiating the mother, is responsible for teratogenesis.

Four photographs; 1 chart; 2 tables.

DONALD F. LOEFFLER, M.D.
University Hospitals, Cleveland, Ohio

The Indirect Effect of Irradiation on Embryonic Development. II. Irradiation of the Placenta. Robert L. Brent. J. Dis. Child. **100:** 103–108, July 1960. (Jefferson Medical College, Philadelphia 7, Penna.)

Direct irradiation of the embryo has for some time been known to cause congenital malformations. An attempt was made by the author to determine whether or not irradiation of the placenta alone would cause the same effects as irradiation of the uterus. A unique method of shielding the embryo and irradiating only the placenta was devised.

Five groups of rats were used: a control group; one with irradiation of the placenta only; one with irradiation of the embryo only; one with irradiation of one-half the placenta and one-half the embryo; one with irradiation of the entire embryonic site. A total of 400 r was given to the last four groups on the twelfth day of pregnancy, and the animals were sacrificed on the sixteenth day. The maternal organism received no irradiation in this study.

The groups in which the embryo received radiation displayed congenital malformations, while the control group and the group with irradiation of the placenta alone showed no abnormalities.

Again, this substantiates the conclusion that direct ionizing irradiation of the embryo is needed for the production of congenital malformations. The direct effects of ionizing irradiation are not a result of placental injury, nor are they caused by metabolic abnormalities induced in the mother by irradiation of the maternal organism (see preceding abstract). Fetal growth and fetal mortality were not affected by placental irradiation.

One roentgenogram; 2 diagrams; 2 tables.

DONALD F. LOEFFLER, M.D.
University Hospitals, Cleveland, Ohio

Serum Enzymes Following Whole-Body Radiation in the Rabbit. Harry G. Albaum. Radiation Res. 12: 186–194, February 1960. (Brooklyn College, Brooklyn, N. Y.)

A series of enzymes were studied in sham and x-irradiated rabbits to determine (1) whether any other single enzyme could be used as a better early indicator of irradiation trauma than glutamic oxalacetic transaminase; (2) whether irradiation is able to inactivate normally occurring serum enzymes; (3) whether in a large group of different assays, any pattern of change, not necessarily marked for any single enzyme, may be apparent within twenty-fours after radiation exposure.

The author presents data on alterations in serum enzyme activity following whole-body x-irradiation of rabbits at a dosage level of 750 r. Of 14 enzymes investigated, no single one was found to be a better early indicator of irradiation trauma than glutamic oxalacetic transaminase. At least 3 of the enzymes were significantly lower in the serum of the irradiated animals six hours after exposure than they were in the sham controls, suggesting either inactivation or interference with synthesis.

Of the 14 enzymes studied, 4 were significantly elevated, 3 were lowered, and 7 remained unchanged within twenty-four hours after irradiation.

Studies on the Mechanism of Secondary Disease. The Parental-F_1 Hybrid Radiation Chimera. Leonard J. Cole and Richard M. Garver. Radiation Res. **12:** 398–408, April 1960. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

The authors employed the parental-F_1 hybrid lymphoid radiation chimera as a test system for measuring or assaying the functional status of lymphoid tissue after irradiation.

A lethal wasting syndrome was elicited in sublethally x-irradiated (500 r) LAF_1 hybrids, not only when A-strain spleen cells (25×10^6) were injected immediately after irradiation, but also after an interval of eight, fifteen, or twenty-two days postirradiation. Apparently, functional lymphoid recovery has not as yet occurred at this time, in spite of recovery of spleen cellularity by twenty-two days. At thirty-five and forty-seven days after 500 r, the F_1 hybrids were able to survive after injection of spleen cells.

Injection of A-strain cells into nonirradiated LAF_1 young adult recipients (nine to fifteen weeks of age) did not elicit deaths; by contrast, administration of A-strain spleen cells into nonirradiated old LAF_1 mice elicits deaths, with concomitant histological evidence of lymphoid tissue degeneration.

On the basis of the above findings, a mechanism of production of the lethal syndrome is proposed, and some consequences with respect to the general problem of secondary disease are discussed. It is suggested that secondary disease involves a continuous, dynamic, mutual cell-to-cell homograft reaction between donor and host lymphoid cells, which results in killing of both donors and host lymphoid cells, and in an animal with atrophic lymphoid tissues. The hypothesis accounts for the differential in lymphoid regeneration in lethally x-irradiated recipients after isologous versus nonisologous marrow therapy. Deaths in the old nonirradiated LAF_1 mice injected with A-strain spleen cells is attributed to a relatively deficient lymphoid tissue regenerative potential, as compared to that of young adult mice.

Four tables. AUTHORS' SUMMARY

The Effects of Total-Body Irradiation of Dogs with Simulated Fission Neutrons. E. L. Alpen, O. S. Shill, and E. Tochilin. Radiation Res. **12**: 237–250, March 1960. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

Mongrel male dogs were exposed to neutrons obtained by bombarding a thick Be target with 12-Mev protons. The distribution of neutron and associated x-ray dose was measured throughout the volume of a tissue-equivalent phantom constructed to simulate an average dog. The median lethal mid-line tissue dose was 239 rads, of which 165 rads was from neutrons and 74 was from γ-rays. The potency ratio, compared with 250-kvp x-rays, was approximately 0.9, in good agreement with the value of 0.95 found by other workers with a higher energy neutron beam. The significance of this potency ratio in terms of the gastrointestinal and bone marrow-injuring potential of neutrons is discussed, and the idea is presented that death after neutron irradiation of dogs is almost purely the result of bone-marrow injury, whereas death in rodents is the result largely of injury to the gastrointestinal tract.

Seven figures; 4 tables. AUTHORS' SUMMARY

Modes of Radiation Death in the Chick Embryo. I. Acute Syndromes. S. P. Stearner, M. H. Sanderson, E. J. Christian, and S. A. Tyler. Radiation Res. **12**: 288–300, March 1960. (Argonne National Laboratory, Lemont, Ill.)

In the chick embryo irradiated after six days of incubation, mortality within twelve days following acute exposures to Co^{60} γ-irradiation roughly falls into three intervals—zero to one day, two to five days, and six to twelve days. These time periods are closely correlated with the appearance of certain grossly visible pathologic conditions observed in decedents. The pooling of blood in the large veins is associated with deaths occurring within twenty-four hours after irradiation. Localized accumulations of fluid are principally characteristic of deaths between two and five days, whereas hepatic lesions as well as evidence of hematopoietic failure predominate among deaths between six and twelve days. This association between observed pathology and mortality period suggests a method of partitioning the acute effects that are expressed within twelve days after irradiation. Deaths occurring within each of the three nonoverlapping periods are assumed to represent the attainment of lethal bounds by independent injury processes, the kinetics of which are reflected in the joint behavior of the experimental variables associated with deaths within that period.

Seven figures; 1 table. AUTHORS' SUMMARY

Modes of Radiation Death in the Chick Embryo. II. A Model of Lethal Mechanisms. S. A. Tyler and S. P. Stearner. Radiation Res. **12**: 301–316, March 1960. (Argonne National Laboratory, Lemont, Ill.)

In another paper of this series (see preceding abstract) a close correspondence was reported between the dominant acute pathology observed at death in γ-irradiated chick embryos and the interval of time at which death occurs. In the experiments described here the time interval in which a radiation death occurs was used as the discriminating criterion for isolating modes of injury. A statistical analysis was made of the interrelationships between dose, exposure time, and observed mortality for each of the time periods.

Among six-day chick embryos, the mortality observed within twelve days after an acutely lethal irradiation with Co^{60} γ-rays was partitioned into three groups based on survival time, as in the earlier studies. A statistical analysis revealed that dose, exposure time, and mortality could be simply related within each post-irradiation period. Statistical results together with the pathology observed in decedents suggested the following characterization as a possible model of the mechanisms that influence significantly the acute radiation syndrome:

1. Radiation effects which initiate an injury that leads to mortality in the first period (zero to one day) are reversed at a constant rate. Vascular collapse was observed as the dominant pathology among decedents of this period.

2. Mortalities occurring in the second period (two to five days) reflect lethal injuries that are sustained *via* either a reversible or an irreversible process or both. Fluid imbalance describes grossly the pathological expressions of sustained lethal injury.

3. Hepatic lesions and hematopoietic failure are typical indicators of radiation damage among decedents of the third period (six to twelve days). Radiation effects that produce an insult that is lethal in this period are irreversible.

An alternate model that postulates a single percursory mechanism on which the injury process of the first period and the reversible process of the second period is summarized.

For the embryo and young chick, the reversal processes of the first period are descriptively and pathologically similar.

Nine figures; 3 tables.

The Relative Biological Effectiveness of Cobalt-60 Gamma Rays and 220-Kvp X-Rays on the Viability of Chicken Eggs. Merle K. Loken, Arthur A. Beisang, Eugene A. Johnson, and Donn G. Mosser. Radiation Res. **12**: 202–209, February 1960. (University of Minnesota Hospitals, Minneapolis 14, Minn.)

The relative biological effectiveness (RBE) of cobalt-60 γ-rays and 220-kvp x-rays was determined by using previously unincubated fertile chicken eggs. The criterion chosen to demonstrate RBE was the percentage of irradiated eggs that did not hatch. The RBE with 95 per cent confidence interval was found to be 0.82 ± 0.06 when the absorbed dose was measured at the position of the embryo. On the basis of absorbed dose rate determined at the center of the egg, the RBE was 0.80 ± 0.06.

The relative biological effectiveness was independent of dosage in the range from 330 to 1,030 rads.

The LD 50's for cobalt-60 γ-rays and 220-kvp x-rays were determined to be 705 ± 21 and 583 ± 17 rads, respectively. These values were obtained from measurements of absorbed dose at the position of the embryo.

One figure; 1 table.

Studies on the Effects of Radiation on Living Cells in Tissue Culture. I. Radiosensitivity of Various Imaginal Discs and Organs in Larvae of Drosophila melanogaster. Masakatsu Horikawa and Tsutomu Sugahara. Radiation Res. **12**: 266–275, March 1960. (National Institute of Genetics, Mishima, Japan)

In order to study the effect of x-irradiation on larvae of *Drosophila melanogaster* various imaginal disks and organs of third-instar larvae were cultured in a synthetic

medium (K-6) together with cephalic complexes as a source of the metamorphic hormone. Irradiated disks or organs were used for culture in one series and irradiated cephalic complexes were employed in the other. From the differences in results obtained in the two series the authors conclude that the decrease in per cent ecdysis which was observed was caused by a functional disturbance of the cephalic complex induced by irradiation. It was found that the brain, the wing disk, and the testis were more radiosensitive than the eye disk, the leg disk, the salivary gland, and the fat body.

Five figures; 1 table.

The Relative Biological Effect of Various Qualities of X-Rays on Growth of Ascites Tumor Cells. Norman A. Baily and Ruth A. Brother. Radiation Res. **12**: 389–397, April 1960. (Roswell Park Memorial Institute, Buffalo, N. Y.)

The relative biological effectiveness (RBE) of x-ray beams of various quality, ranging in half-value layers from 0.25 mm. Al to 7.6 mm. Pb, was determined by studying the inhibition of ascites tumor cell growth in Swiss mice. In this biological system, no significant difference in RBE was detected over the range of x-ray qualities used.

One figure; 4 tables. AUTHORS' SUMMARY

Effect of X-Radiation on DNA Metabolism in Various Tissues of the Rat. II. Recovery after Sublethal Doses of Irradiation. Oddvar F. Nygaard and Richard L. Potter. Radiation Res. **12**: 120–130, February 1960. (R. L. P., University of Michigan Medical School, Ann Arbor, Mich.)

In a previous report (Radiation Res. **10**: 462, 1959. Abst. in Radiology **74**: 528, 1960) the authors described the inhibition of the synthesis of desoxyribonucleic acid (DNA) in various rat organs during the first twenty-four hours after x-irradiation. The present report is concerned with the effect of 100 r and 400 r of total-body x-irradiation on DNA synthesis in thymus, spleen, and small intestine of the rat over extended periods. The incorporation of thymidine-2-C^{14} into DNA during one hour was used as a relative measure of DNA synthesis.

Following an initial period of inhibition the tissues recovered their ability to synthesize DNA. The time for this recovery depended on the tissue and on the radiation dose. In terms of specific activity of the isolated DNA, *i.e.*, the relative rate of DNA synthesis, the maximum rate of recovery after 100 r for small intestine, spleen, and thymus was at two, two, and three days, respectively. After 400 r the maximum specific activities were observed at two, six, and four days for the same tissues, the spleen in this case recovering later than the thymus. Since there was an extensive initial loss of DNA from the irradiated organs, the recovery in terms of total activity of the DNA was less pronounced than that of the specific activity.

In all cases the specific activity exceeded the control value at the time of maximum recovery, usually by a factor of approximately 2. For thymus after 400 r this "overshoot" was ten times as great as the control value, indicating an extremely active regeneration.

The authors conclude that the effect of irradiation on the DNA metabolism of the three tissues studied can be considered qualitatively the same, differing only in the degree of acute cell death, in the duration of the delay of DNA synthesis in the surviving cells, and in the rate of recovery resulting from accelerated cell replication during the period of regeneration.

Three figures.

Effect of X-Radiation on DNA Metabolism in Various Tissues of the Rat. III. Retention of Labeled DNA in Normal and Irradiated Animals. Oddvar F. Nygaard and Richard L. Potter. Radiation Res. 12: 131–145, February 1960. (R. L. P., University of Michigan Medical School, Ann Arbor, Mich.)

In previous communications (see preceding abstract) the effect of x-irradiation on the synthesis and the amount of DNA in thymus, spleen, and small intestine of the rat was considered. The investigation described here concerns the fate of the DNA of these organs after 100 r and 400 r of total-body irradiation. For this purpose the retention of DNA was studied in normal animals and in animals irradiated three hours or twenty-four hours after the injection of a radioactive precursor. Thymidine-2-C^{14} proved of unique value as a labeling agent, since its incorporation is complete after a relatively short time and the radioactivity is not retained in any cell constituents other than DNA.

From the results obtained in the normal rats average turnover times were calculated for the more active cells in thymus, spleen, bone marrow, and small intestine. The data also provided a rough estimate of the migration time of the epithelial cells in the small intestine.

The specific activity of the DNA retained in the different organs of the irradiated animals indicated that the labeled and unlabeled cells were lost in an essentially random manner. This suggests that, with respect to the *loss of cells* from these organs, the dividing and nondividing cells are, on the average, equally sensitive to irradiation. There was no indication of cyclic changes in this sensitivity nor did the cell loss appear to relate to any specific time of the division cycle.

Nine figures.

Protective Effects on Fecundity and Fertility from Feeding Cysteine and Glutathione to Habrobracon Females before X-Irradiation. Daniel S. Grosch. Radiation Res. **12**: 146–154, February 1960. (North Carolina State College, Raleigh, N. C.)

The author reconsiders the first compounds discovered to afford protection to irradiated rats, *i.e.*, cysteine and glutathione, by employing them to influence the reproductive capacity in an insect with polytrophic ovarioles (the small parasitoid wasp *Habrobracon*). This permits the contrasting of responses among differing but related cell types.

Protective effects on oviposition and egg hatchability were shown for both cysteine and glutathione when fed to female wasps before x-irradiation. The effect, detected only during a period three to twelve days after treatment, was therefore limited to cells in transition from oögonia to differentiated trophocyte-oöcyte units. Transition involves completion of a series of mitotic divisions. Although a direct effect on cell division may be reflected in the number of eggs produced per unit of time, a response deferred until the crises of embryonic development implies alteration in the genetic rather than the kinetic mechanism. Indeed, both the effects on oviposition and egg hatchability could trace back to modifications of chromosomal damage, immediate and delayed.

Two figures; 3 tables.